

#33/dec.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: WALLACH=23

In re Application of:) Conf. No. 2755
)
David WALLACH et al) Art Unit: 1635
)
Appln. No.: 09/380,546) Examiner: B. Whiteman
)
Filed: November 29, 1999) Washington, D.C.
)
For: CASH (CASPASE HOMOLOGUE))
WITH DEATH EFFECTOR DOMAIN,)
MODULATORS OF THE FUNCTION)
OF FAS RECEPTORS)

DECLARATION UNDER 37 CFR §1.131

Honorable Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Yura "Yury" GOLTSEV, hereby declare and state as follows:

I am the same Yura Goltsev named as a co-inventor in the above-identified application and my educational and professional experience is presented in the curriculum vitae attached hereto as Exhibit A.

The experiments and computer searches described below were either conducted by me or under my supervision, and I can attest of my own personal knowledge that all the results reported herein and the dates ascribed thereto are true and accurate.

It is my understanding that the claims of the above-identified application remain rejected under 35 U.S.C. §102(e) as being anticipated by Shu et al., U.S. Patent No. 6,242,569. The filing date of U.S. Patent No. 6,242,569 for purposes of §102(e) is February 5, 1997.

The present declaration is intended to establish that the invention of the subject matter of the rejected claims was made on or before the effective filing date of U.S. Patent No. 6,242,569. The following shows conception on or before February 5, 1997, and diligence until the filing of Israeli patent application IL 120367, from which the benefit of foreign priority is claimed in the above-identified application, on March 3, 1997, as a constructive reduction to practice.

The dates of the experiments and computer searches to show conception are excised but every excised date is on or before February 5, 1997. Furthermore, the experiments and computer searches were done in Israel, a WTO member country, on or after January 1, 1996.

Attached hereto as Exhibit B are pages 106, 107 and 110 of my laboratory notebook (with the dates excised) with entries made by me in my own handwriting. Page 106 shows a two hybrid (2H) screen of MCH4L with a Jurkat library (in GAD1318 vector) without 3AA and restriction enzyme digests of

clones obtained from the Jurkat library. A continuation of the restriction enzyme digests of the clones from the Jurkat library is shown on page 107. The heading for page 110 is "Cloning of G1 isoforms", where the clones were obtained from RT-PCR of HeLa pA RNA. Restriction enzyme digestions of the clones are shown on page 110, where the "circled" clones were sequenced.

To clarify the terminology used for the polypeptide of the present invention, the G1 α isoform (long splice variant) of SEQ ID NO:2, encoded by the nucleotide sequence of SEQ ID NO:1, is also referred to as CASH α or CASHa, as will be seen in some Exhibits presented herein. Likewise, the G1 β isoform (short splice variant) of SEQ ID NO:4, encoded by the nucleotide sequence of SEQ ID NO:3, is also referred to as CASH β or CASHb.

Two nucleotide sequences, designated j13.1789 and j15.1789, obtained from the G1 isoform clones are shown in Exhibit C. These two nucleotide sequences overlap (but on different strands) to give the nucleotide sequence of the short variant G1 β isoform (CASH β or CASHb).

For purposes of showing the relationship of the sequences j13.1789 and j15.1789 to CASHb, a color schematic diagram, which is not intended to be to scale, is presented as Exhibit D, where each color represents regions of sequence

identity. The vertical lines starting from the left indicate the start of the coding sequence for CASHa and CASHb, the end of the region of similarity between CASHa and CASHb, the end (bSTOP) of the coding sequence of CASHb, and the end (aSTOP) of the coding sequence of CASHa. As can be seen from this schematic diagram, the nucleotide sequences of j13.1789 and j15.1789 cover the entire coding sequence of CASHb. The sequences labeled with accession numbers AA149562, AA151642, N94588, and W23795 are contigs identified for CASHa and CASHb that were available in the GenBank (NCBI) sequence database prior to the date the invention was made. The sequence database printouts for these contigs are presented as Exhibit E.

Part of the sequence from j15.1789 was used in a BLAST search for identification of similar protein coding regions in the GenBank database. The BLAST search results are presented as Exhibit F and the 313 base pair query sequence used in the BLAST search is shown in Exhibit G.

To search for other splice variants (which is routinely done in the art) of CASHb, a 219 base pair query sequence from j13.1789, shown as Exhibit H, was used in a BLAST search (Exhibit I) for identifying from the GenBank EST database, ESTs with nearly identical sequences. As shown in Exhibit I, the EST sequences with accession numbers AA149562

and AA15142 (highlighted) were identified. The yellow highlighting is not part of the original document and was made contemporaneously herewith to aid the examiner's understanding of this document. EST accession numbers AA149562 and AA151642 are the same accession numbers shown in Exhibit D to generate contigs for the coding sequence of CASHa. Accordingly, from the j15.1789 and j13.1789 sequences generated from the G1 isoform clones and the contigs identified based on BLAST sequence similarity searches, as summarized in Exhibit D, the nucleotide sequences and the encoded amino acid sequences for CASHa and CASHb were obtained, and therefore the present invention was conceived on or before February 5, 1997.

A printout from the "Sequencher" program dated February 8, 1997, supplemented with my hand made drawings on the printout, is attached hereto as Exhibit J. This printout is a contig of ESTs for CASHa and CASHb which lists more ESTs as well as contigs from The Institute for Genomics Research (TIGR) database that have regions coinciding with the CASH sequences.

As the sequences of both the short and long splice variants of CASH (CASHb and CASHa) were obtained by a combination of overlapping clones and contigs identified from a search of an EST sequences database, I set out to confirm the sequence for both CASHb and CASHa by ordering the

synthesis of oligonucleotide primers for use in sequencing/PCR. An ordering form with the heading "Oligos for G1" dated February 9, 1997, and showing the oligo primers ordered, with my handwriting on the side to indicate the identifying number for each the primers ordered, is attached hereto as Exhibit K.

Exhibit L is an updated version of Exhibit J. While it is undated, it was attached to the ordering form dated February 9, 1997, herein presented as Exhibit K. At the bottom of Exhibit L, I had noted in my own handwriting the approximate positions of the oligo primers, i.e., 18046, 18044, etc., first identified in Exhibit K.

Pages 111-113 from my laboratory notebook are attached hereto as Exhibit M, where page 111 shows an analysis of cDNA clones containing CASH sequences recovered from a library and page 112 shows restriction enzyme digests of plasmids containing cDNA fragments subcloned from the clones presented on page 111. While page 111 is undated, I performed this experiment either before or contemporaneously with the experiment on page 112. Page 113, also undated, shows a restriction enzyme analysis of plasmids expressing deletion mutants of CASH.

Attached hereto as Exhibit N is the printout from a BLAST search of the GenBank EST database using a 139 base pair

sequence from murine CASH as the query sequence. Note that on page 3 of this printout the BLAST search was conducted on February 16, 1997.

The sequences identified by 10609.1818, 11717.1818, and 18648.1818, dated February 25, 1997, and attached hereto as Exhibit O, are from sequencing a CASHb expression vector using three different primers, one of which (primer 18648) is shown on the oligo ordering form presented as Exhibit K.

Similarly, sequencing of a CASHa expression vector yielded the sequences identified by rti-651.1831 and rtl-648.1831, dated March 3, 1997, and attached hereto as Exhibit P.

The sequences of some "V" clones containing CASH (both long and short) obtained from cDNA library screening, dated February 25, 1997, are presented in Exhibit Q.

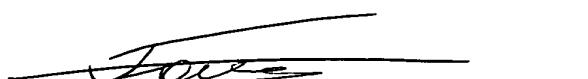
Exhibit R, attached hereto, presents three sheets that were attached together in my datafile. The first page is an undated schematic hand made drawing of V clones containing CASH (both long and short). The second page is a "Sequencher" contig, dated February 26, 1997, of ESTs and the sequences of some the V clones. The third page, dated February 27, 1997, is a more expanded contig including ESTs and the sequences for V clones.

In conclusion, the conception of the present invention occurred on or before February 5, 1997, and there was diligence from February 5, 1997, the date of filing of U.S. Patent No. 6,242,569, until the March 3, 1997, filing of Israeli patent application IL 120367 as a constructive reduction to practice. Accordingly, the applied Shu et al. reference, U.S. Patent No. 6,242,569, is antedated and withdrawal of the 35 U.S.C. §102(e) rejection is warranted.

The undersigned declares further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

27 May 2003

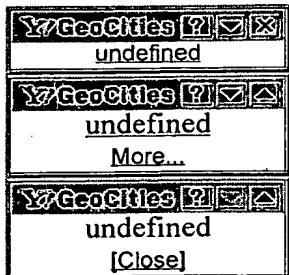
Date


Yura Goltsev

09-380546

#33

Exhibit A



CURRICULUM VITAE

Yury V. Goltsev

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EDUCATION:

1989-1993:	Bachelor of Science Moscow Institute for Physics and Technology Majors in Physical Chemistry and Biophysics
1993-1995:	Master of Science Moscow Institute for Physics and Technology Subject area: Molecular Biophysics
1995-2002:	Ph.D. in Molecular Biology The Weizmann Institute of Science Supervisor: Prof. David Wallach Thesis topic: Novel approaches to identification of signaling molecules activated by receptors of the TNF/NGF family, and their application to the study of cFLIP/CASH

DATE OF BIRTH: June 10th, 1972

MARITAL STATUS: married, two children

CITIZENSHIP: Israel

MY REFEREES ARE:

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<http://www.biu.ac.il/LS/staff/michaeli.html>

AREA OF SCIENTIFIC EXPERTISE:

Last six years: Molecular analysis of cytokine-induced signal transduction pathways, in particular those triggered by the TNF/FAS-family members. Molecular regulation of apoptosis.

TECHNICAL SKILLS:

Recombinant DNA: conventional molecular cloning techniques, RT-PCR, site-directed mutagenesis, construction of cDNA libraries, DNA & RNA expression analysis (electrophoresis, hybridization, protection, etc), library screening, subtraction by Representation Difference Analysis (RDA)

Mammalian Cell Culture: routine, expression of recombinant protein in culture cells (both transient & stable), analysis: Western, Far Western, immunocytochemistry, GFP visualization system, essential flow cytometry and sorting, ELISA.

Signaling-related Techniques: EMSA & reporter assays for transcription, *in vitro* kinase assay (in gel & in solution), cell viability assays (biochemical and visual), *in vivo* labeling, *in vivo* signal transduction pathway reporting systems (e.g. PathFinder from Stratagene).

Protein-protein Interactions Assays: yeast two- and three-hybrid systems; mammalian interaction traps, *in vitro* pull-down, *in vivo* co-immunoprecipitation (both endogenous and transfected proteins).

Proteomics: Tandem Affinity Purification (TAP) of protein complexes and identification of the components by microsequencing.

Bacterial Expression: Introduction and affinity purification of recombinant proteins, essential HPLC (gel filtration, ion exchange)

PUBLICATIONS:

Boldin, M. P., Goncharov, T. M., Goltsev, Y. V., and Wallach, D. (1996). Involvement of MACH, a novel MORT1/FADD-interacting protease, in Fas/APO-1- and TNF receptor-induced cell death, *Cell* 85, 803-15.

Goltsev, Y. V., Kovalenko, A. V., Arnold, E., Varfolomeev, E. E., Brodianskii, V. M., and Wallach, D. (1997). CASH, a novel caspase homologue with death effector domains, *J Biol Chem* 272, 19641-4.

Wallach, D., Boldin, M., Goncharov, T., Goltsev, Y., Mett, I., Malinin, N., Adar, R., Kovalenko, A., and Varfolomeev, E. (1996). Exploring cell death mechanisms by analyzing signaling cascades of the TNF/NGF receptor family, *Behring Inst Mitt*, 144-55.

Wallach, D., Varfolomeev, E. E., Malinin, N. L., Goltsev, Y. V., Kovalenko, A. V., and Boldin, M. P. (1999). Tumor necrosis factor a receptor and Fas signaling mechanisms, *Annu Rev Immunol* 17, 331-67.

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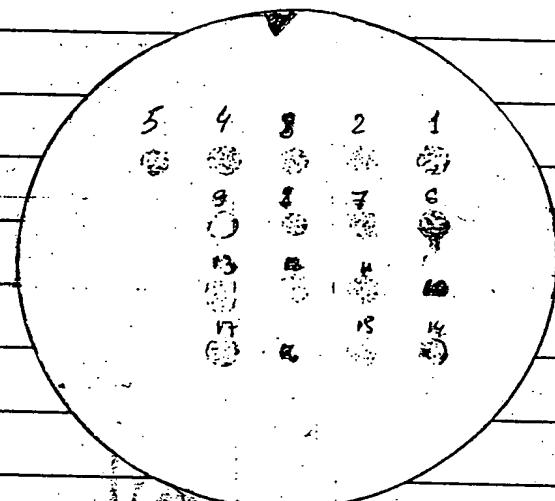
**As rescanning documents *will not* correct images,
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Exhibit B

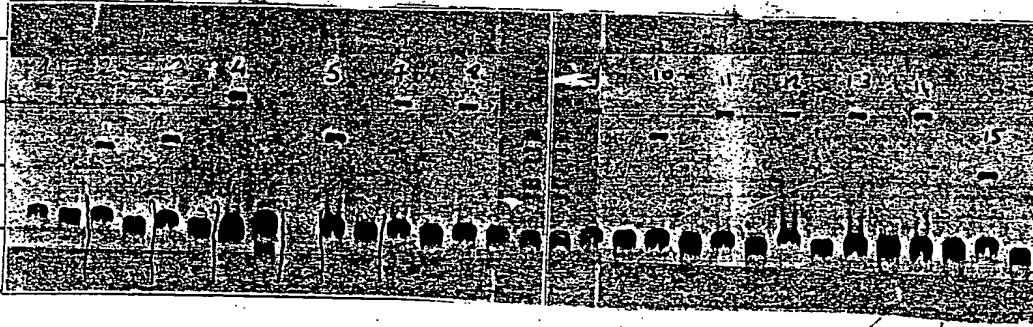
106

24 racen MCML with Jackat Library (in GAD 138)
without 3AA. Initial transform off 2000.000 (without
picked 1100.000 revival)

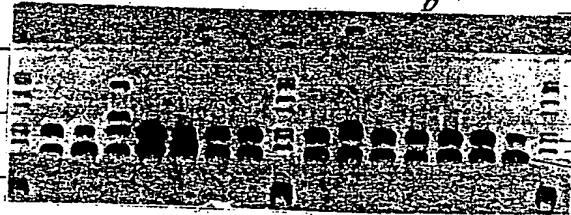
17 became blue in 1h. Secondary testing of here 17



Restriction / 21/10/1



test / Note + Obj I



DATE

Y1 Y2 Y3 Y4

Y5

Y6

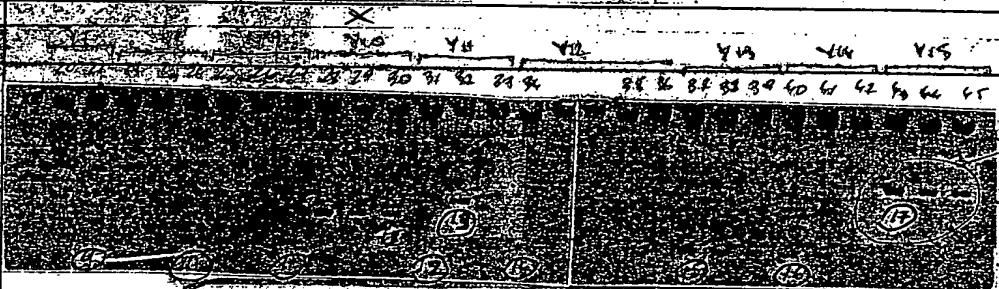
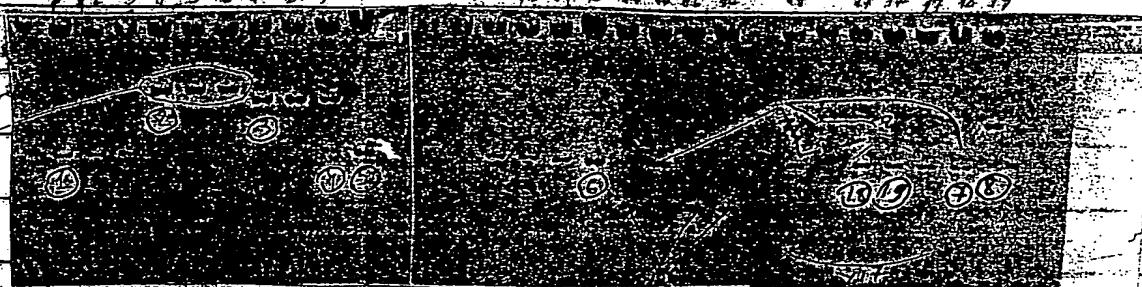
Y7

A1 3 4 5 6 7 8 9 10

A 11 12 13 14 15 16 17 18 19

107

MORE



MORE



Blunting (by T4 DNA polymerase)

25 μl DNA + H₂O

3 μl Buffer

2 μl dNTP

0.5 μl T4

Endonuclease 10 μl 15-30 min

Kinasing (Phosphorylating) (from Red Protocol)
(for 30 μl reaction)

Promega

10 pmol adaptors

50 mM Tris-HCl pH 7.5

5 μl K₄₀ ATP10 mM MgCl₂

5 mM DTT

37°C 1h

Maniatis

1-10 μl diphosphate

1 mM ATP

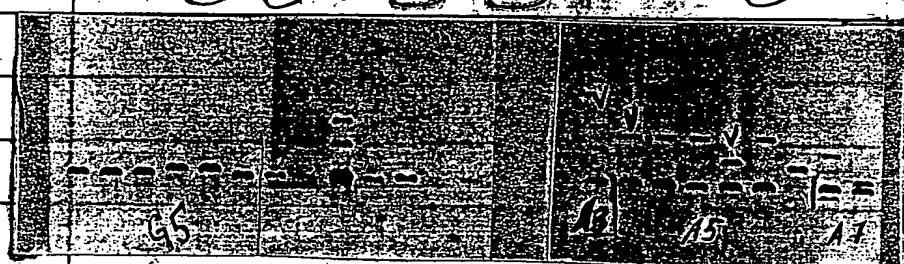
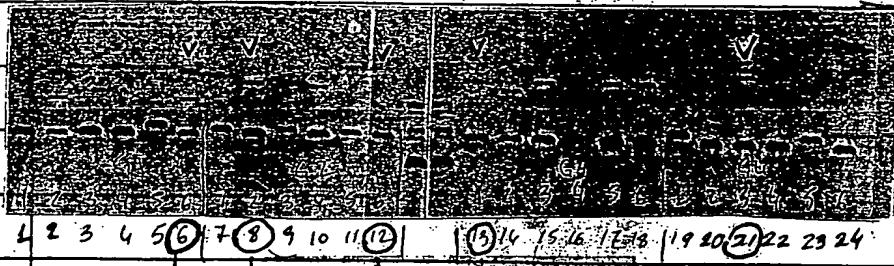
50 μg/ml BSA

20 U T4 polynucleotide kinase

Cloning G1 isoforms / β 2 Xho

110

clones from
RT-PCR on
HeLa -pA RNA

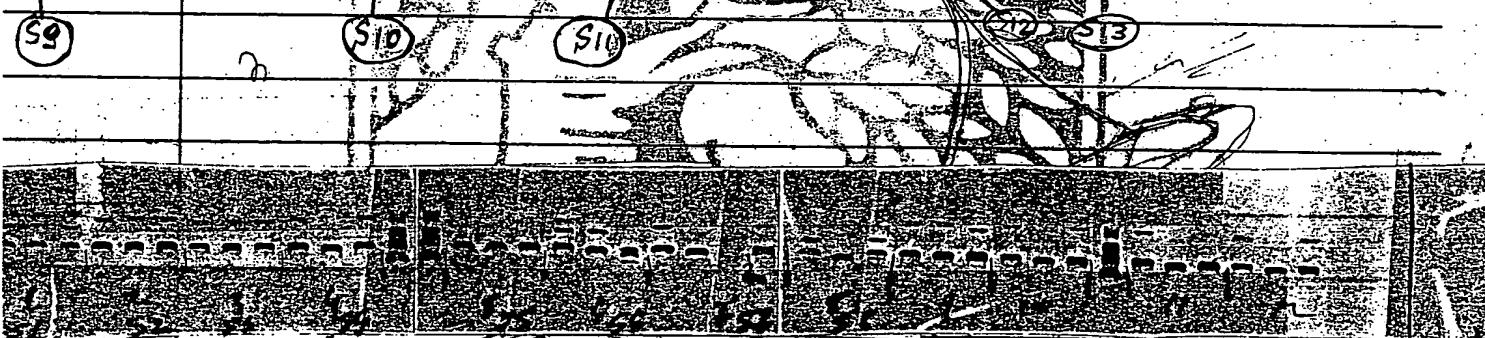


26 27 28 29 30

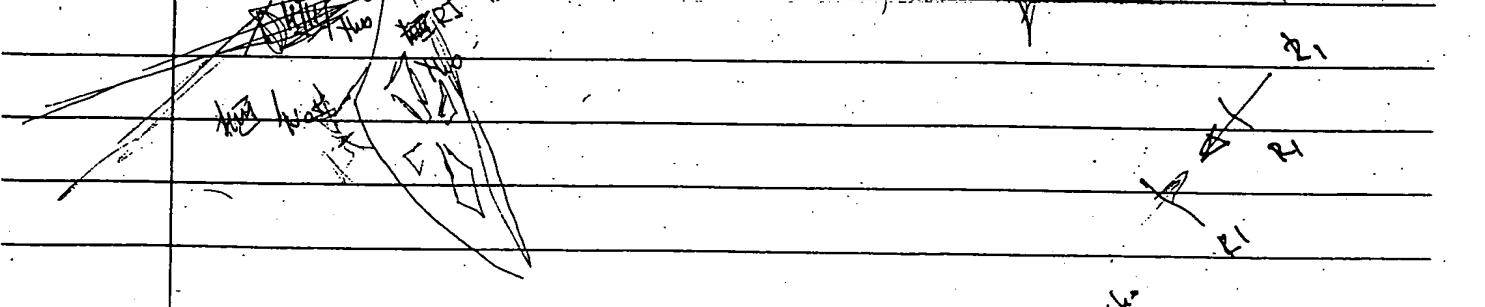
26 27 28 29 30



31 32 33 34 35 36



37 38 39 40 41 42



43 44 45 46 47 48

ID: j13.1789 our Ref: SampleB-1789 27
7.89.seq Leng.: 929

Type: N Check: 3143 ..

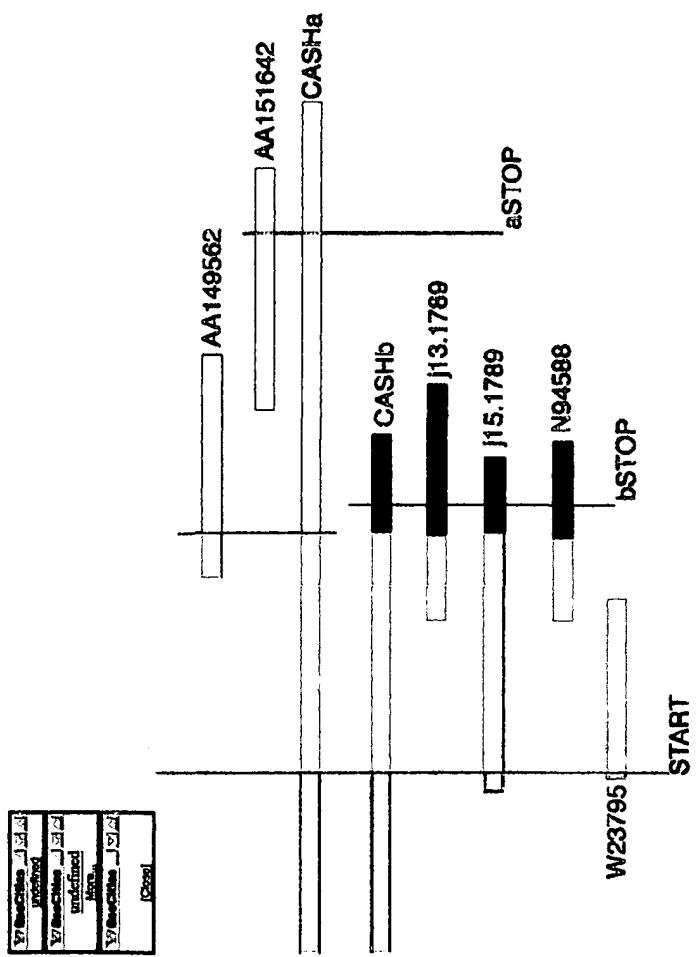
1 CGATTCA TAG ATCAGGGTTT TCCCAGTCAC GACGTTGTA AACGACGGCC
51 AGTGGAAATTG TAATACGACT CACTATAGGG CGAATTGGGT ACCGGGCC
101 CCCTCGAGGT CGAGCGGCCG CAGGGAAATT TTTTTTTTT TTTTTTTTT
151 TTTTTTTTT AAAAAGTACA AGGGATATT ATTATTAAGC ATTATTAGTA
201 gTAACAAAAG ATTGGAAAGC ATCTAACAT ACAGCAACAA gAAAGGGCTa
251 aACACATTAT aACaCATTa GAAAATGAAA CGATTTAACtC aTTCCCAATG
301 ATAAANTTNA GGCATTCCAT NTTNNNCACA TGGAANAATT TCCANNCAAT
351 TTTCNATCA TGACAGGGGG CTTNGGGTGT TNTCTNCCTN AANTTTTTN
401 AAGGATCCTT NAAACTCTT TGGATTGCTG CTTGGANAAA NTTCCGTAA
451 CTTGTCCCTG CNCCTATNAA NNGANTGCAG GGTACTTCTG GATTTTGTC
501 TTCAGGTCTA TTCTGTGGAT GTTCTTTAGG CATTTCCTA ATAAATCCCT
551 TGATCTGGGG CCCCCAATT ANTTCTCCC ACTCAACCAC AAGGTCCAAA
601 AAACTCTTCT CCNNGCTTAT CTGCCTEGG CCCCCTGTTTC CTTCCTTGAN
651 GAAAATTATN ANGACNCTCC CATTTCNA NTCCTCCCCA TCTCTGCCAT
701 CACCCCTCTAT TTCCNAAACA AGGTGANGGT TCTTACCAAGG TGGGTTCCCN
751 CNCNTTCTN TCCTCTTCNA AANACTTTGA NCGGTCCNNT CCCCCCCNTT
801 TAANATNCAC CANTCCCCAC CAAAAATTTC TCTTNCCNT CAATTCCAAA
851 GTCCNGNCTT AGGTGACCCA CTTCCANCN CCGGCCNNAA AANACNCCCC
901 CCCCCNTTTA GTTCCCTCCC CTGAAGGTN

Exhibit C

your ID: j15.1789) our Ref: SampleB-1789 22
j15.1789.seq Length: 928) Type: N Check: 7805 ..

1 CCCACCAAAAC CAAAAAAAGA GNCCTAGAAC TAGTCG ~~GAAGCAGG~~ GGGCACGAG
51 GTGTCTGCTG AAGTCATCCA TCAGGTTGAA GAAGCACTTG ATACAGATGA
101 GAAGGAGATG CTGCTCTTT TGTGCCGGGA TGTTGCTATA GATGTGGTTC
151 CACCTAATGT CAGGGGACCT TCTGGATATT TTACGGGAAA GAGGTAAGCT
201 GTCTGTCGGG GACTTGGCTG AACTGCTCTA CAGAGTGAGG CGATTGACC
251 TGCTCAAACG TATCTTGAAG ATGGACAGAA AAGCTGTGGA GACCCACCTG
301 CTCAGGAACC CTCACCTTGT TTCGGACTAT AGAGTGCTGA TGGCAGAGAT
351 TGGTGAGGAT TTGGATAAAAT CTGATGTGTC CTCATTAATT TTCCTCNTGA
401 AGGATTACAT GGGCCGAGGC AaNAtaATCA AGGAGAAGAN TTTCTGGAC
451 CTTGTGGTTG AATTGGGAGA AACTAAATCT GGTTGCCCN CNATCAACTG
501 GATTTATTAT AAAAATGCCT AAAGAACTCC CCCCANTANA CCTGAAGACA
551 AAAATCCANA ANTACTTCTN TCTGTNCNCG GANCANGGAC GANTTNCTNG
601 AATGTCTCC TANCANCATC CNTNAGAATC TCCANGATCC TTCCNNTNAC
651 TTCNNNGATGA TACCCCTNTC CCCNTGTCCCT NATCTGAAAT TCTGGAAATT
701 GTCCATNTAA TTACNTGGAC TGCCCTNCNT TATCTTCNGN AACNAATAAA
751 TCTTCCCTNC CTAATGTTT TNGAGNNTT ACCCTCCCCG TTNCTGTTN
801 TTANATCCTC CCCCCCCTTG TTTCTCTNTT ATTCCNNNAAN ANANTCCCT
851 TCTTTCTTTT NNNNCCCCN NNNNNNATAA NAATNNTCCC CCCCACNCAG
901 GGGGNNCGGC CCCNTCCNT TTTAATT

Exhibit D



Address: 4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108
Tel: 314 286 1800
Fax: 314 286 1810
E-mail: est@watson.wustl.edu

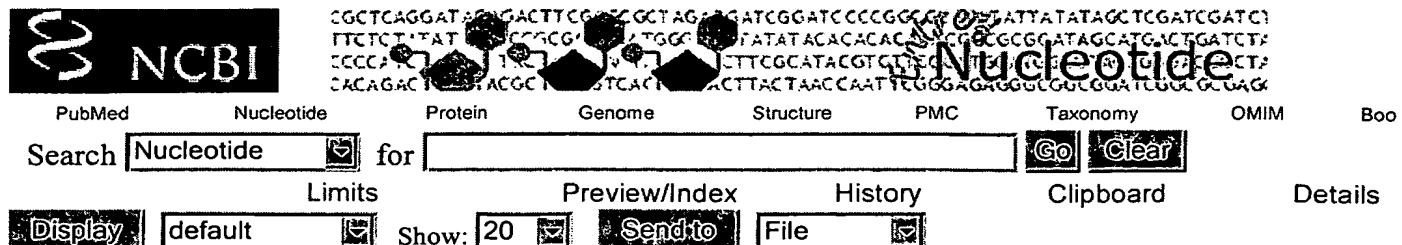
CITATIONS

Medline UID: [97044478](#)
Title: Generation and analysis of 280,000 human expressed sequence tags
Authors: Hillier, L., Lennon, G., Becker, M., Bonaldo, M. F., Chiapelli, B., Chissoe, S., Dietrich, N., DuBuque, T., Favell, A., Gish, W., Hawkins, M., Hultman, M., Kucaba, T., Lacy, M., Le, M., Le, N., Mardis, E., Moore, B., Morris, M., Parsons, J., Prange, C., Rifkin, L., Rohlfing, T., Schellenberg, K., Soares, M. B., Tan, F., Thierry-Mieg, J., Trevaskis, E., Underwood, K., Wohldmann, P., Waterston, R., Wilson, R., Marra, M.
Citation: Genome Res. 6 (9): 807-828 1996

MAP DATA

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Apr 28 2003 10:17:55



PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Boo

Search

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Display Show:

1: AA149562. zo29e05.r1 Strata...[gi:1720363]

Links

IDENTIFIERS

dbEST Id: 788753
 EST name: zo29e05.r1
 GenBank Acc: AA149562
 GenBank gi: 1720363
 GDB Id: 4620622

CLONE INFO

Clone Id: IMAGE:588320 (5')
 Source: IMAGE Consortium, LLNL
 DNA type: cDNA

PRIMERS

Sequencing: -28M13 rev2 from Amersham
 PolyA Tail: Unknown

SEQUENCE

GGAGCAGGGACAAGTTACAGGAATGTTCTCCAAGCAGCAATCCAAAAGAGTCTCAAGGAT
 CCTTCAAATAACTTCAGGCTCCATAATGGGAGAAGTAAAGAACAAAGACTTAAGGAACAG
 CTTGGCGCTCAACAAGAACCGAGTGAAGAAATCCATTAGGAATCAGAAGCTTTGCCT
 CAGAGCATACCTGAAGAGAGATAAAGATGAAGAGCAAGCCCCTAGGAATCTGCCTGATA
 ATCGATTGCATTGGCAATGAGACAGAGCTTCTCGAGACACCTTCACCCCTGGCTAT
 GAAGTCCAGAAATTCTTGCACTCAGTATGCATGGTATATCCCAGATTCTGGCCAATT
 GCCTGTATGCCCGAGCACCGAGACTACGACAGCTTGTGTGTCCCTGGTGGCCAGGA
 GGTCCAGAGTGTGTATGGTGGATCAGACTCACTCAGGGCTCCCTGCATCACATCAG
 GAGGATGTTCATGGGAGAATCATGCCCTATCTAGCAGGAAGCAAAGATGTTTTATC

Quality: High quality sequence stops at base: 398

Entry Created: Dec 10 1996
 Last Updated: Dec 10 1996

COMMENTS

This clone is available royalty-free through LLNL ; contact the IMAGE Consortium (info@image.llnl.gov) for further information.

LIBRARY

Lib Name: Stratagene colon (#937204)
 Organism: Homo sapiens
 Organ: colon
 Tissue type: tumor
 Cell line: T84 carcinoma cell line
 Lab host: SOLR cells (kanamycin resistant)
 Vector: pBluescript SK-
 R. Site 1: EcoRI
 R. Site 2: XhoI

Description: Cloned unidirectionally. Primer: Oligo dT. T-84 colonic epithelial cell line. Average insert size: 1.0 kb; Uni-ZAP XR Vector; ~5' adaptor sequence: 5' GAATTCTGGCACGAG 3' ~3' adaptor sequence: 5' CTCGAGTTTTTTTTTTTTTT 3'

SUBMITTER

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Fax: 314 286 1810
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CITATIONS

Medline UID: [97044478](#)
Title: Generation and analysis of 280,000 human expressed sequence tags
Authors: Hillier, L., Lennon, G., Becker, M., Bonaldo, M.F., Chiapelli, B., Chissoe, S., Dietrich, N., DuBuque, T., Favello, A., Gish, W., Hawkins, M., Hultman, M., Kucaba, T., Lacy, M., Le, M., Le, N., Mardis, E., Moore, B., Morris, M., Parsons, J., Prange, C., Rifkin, L., Rohlfing, T., Schellenberg, K., Soares, M.B., Tan, F., Thierry-Mieg, J., Trevaskis, E., Underwood, K., Wohldmann, P., Waterston, R., Wilson, R., Marra, M.
Citation: *Genome Res.* 6 (9): 807-828 1996

MAP DATA

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Apr 28 2003 10:17:55

[5' TGTTACCAATCTGAAGTGGGAGCGGCCGCATTTTTTTTTTTTT 3'], double-stranded cDNA was size selected, ligated to Eco RI adapters (Pharmacia), digested with Not I and cloned into the Not I and Eco RI sites of a modified pT7T3 vector (Pharmacia). Library went through one round of normalization to a Cot = 5. Library constructed by Bento Soares and M.Fatima Bonaldo.

SUBMITTER

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Institution: Washington University School of Medicine
Address: 4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108
Tel: 314 286 1800
Fax: 314 286 1810
E-mail: est@watson.wustl.edu

CITATIONS

Medline UID: [97044478](#)
Title: Generation and analysis of 280,000 human expressed sequence tags
Authors: Hillier,L., Lennon,G., Becker,M., Bonaldo,M.F., Chiapelli,B., Chissoe,S., Dietrich,N., DuBuque,T., Favello,A., Gish,W., Hawkins,M., Hultman,M., Kucaba,T., Lacy,M., Le,M., Le,N., Mardis,E., Moore,B., Morris,M., Parsons,J., Prange,C., Rifkin,L., Rohlfing,T., Schellenberg,K., Soares,M.B., Tan,F., Thierry-Mieg,J., Trevaskis,E., Underwood,K., Wohldmann,P., Waterston,R., Wilson,R., Marra,M.
Citation: *Genome Res.* 6 (9): 807-828 1996

MAP DATA

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Apr 28 2003 10:17:55



PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM BBO

Search Nucleotide for

Limits Preview/Index History Clipboard

Sh... 20 Send to File

Clipboard

Clear

Details

Display **default** Show: **20** Send to File

□ 1: W23795. zb79a05.r1 Soares...[gi:1300619]

Links

IDENTIFIERS

dbEST Id: 530869
EST name: zb79a05.r1
GenBank Acc: W23795
GenBank gi: 1300619
GDB Id: 1253190

CLONE INFO

Clone Id: IMAGE:309776 (5')
Source: IMAGE Consortium, LLNL
Insert length: 939
DNA type: cDNA

PRIMERS

Sequencing: mob. REGA+ET
PolyA Tail: Unknown

SEQUENCE

AGAGTAGGATGTCGCTGAAGTCATCCATCAGGGTGAAGAAGCACTTGATACAGATGAGA
AGGAGATGCTGCTTTTGTGCCGGATGTTGCTATAGATGTGGTCCACCTAAATGTCA
GGGACCTTCTGGATATTTACGGGAAAGAGGTAAAGCTGTCGTCGCCCCACTTGGCTGAAC
TGCTCTACAGAGTGAGGCGATTGACCTGCTAACGTATCTTGAAGATGGACAGAAAAG
CTGTGGAGACCCACCTGTCAGGAACCTCACCTTGGACTATAGAGTGCTGATGT
CAGAGATTGGTGA

Quality: High quality sequence stops at base: 247

Entry Created: May 9 1996
Last Updated: Aug 20 1996

COMMENTS

This clone is available royalty-free through LLNL ; contact the IMAGE Consortium (info@image.llnl.gov) for further information.

LIBRARY

Lib Name: Soares_senescent_fibroblasts_NbHSF
Organism: Homo sapiens
Tissue type: senescent fibroblast
Lab host: DH10B (ampicillin resistant)
Vector: pT7T3D (Pharmacia) with a modified polylinker V_TYPE:
phagemid
R. Site 1: Not I
R. Site 2: Eco RI
Description: 1st strand cDNA was primed with a Not I - oligo(dT) primer
[5' TGTTACCAATCTGAAGTGGGAGCGGCCGATTTTTTTTTTTTTTT 3'],
double-stranded cDNA was size selected, ligated to Eco RI

adapters (Pharmacia), digested with Not I and cloned into the Not I and Eco RI sites of a modified pT7T3 vector (Pharmacia). Library went through one round of normalization to a Cot = 5. Library constructed by Bento Soares and M.Fatima Bonaldo.

SUBMITTER

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CITATIONS

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Citation: *Genome Res.* 6 (9): 807-828 1996

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Apr 28 2003 10:17:55

Exhibit F

BLAST Search Results with RepeatMasker filtering, Entrez and SRS links

BLAST search performed using the National Center for Biotechnology Information's BLAST WWW Server. Repeat reporting and filtering performed by RepeatMasker from U. Washington.

Links to Entrez and to the Sequence Retrieval System (SRS) provided by the Human Genome Center, Baylor College of Medicine:

- E** = Retrieve Entrez links (e.g., Medline abstracts, FASTA-formatted sequence reports).
- R** = Retrieve Entrez links to Related sequences (neighbors).
- S** = Retrieve SRS links (if present).

Reference: Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. *Nat. Genet.* 3:266-72. Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. *J. Mol. Biol.* 215:403-10.

Notice: statistical significance is estimated under the assumption that the equivalent of one entire reading frame in the query sequence codes for protein and that significant alignments will involve only coding reading frames.

Query= tmpseq_1
(313 letters)

Translating both strands of query sequence in all 6 reading frames

Database: Non-redundant GenBank CDS
translations+PDB+SwissProt+SPupdate+PIR
241,922 sequences; 68,723,500 total letters.

Searching.....done

Sequences producing High-scoring Segment Pairs:		Reading Frame	High Score	Smallest Sum	
				Probability P(N)	N
gi 1718327	(U75698) ORF K13 [Kaposi's sarcom...	+3	121	3.0e-09	1
gi 1492103	(U60315) MC160L [Molluscum contag...	+3	69	7.4e-06	2
pir IIS55668	hypothetical protein E8 - equine ...	+3	66	4.2e-05	2
gi 1492102	(U60315) MC159L [Molluscum contag...	+3	63	9.5e-05	2
gi 1813378	(D86547) still life type 1 [Drosophila melanogaster]	-3	40	0.00040	4
sp P47211 GALR_HUMAN	GALANIN RECEPTOR (GALL-R) /gi 559...	+2	73	0.26	1
gi 58271	(X12896) CTAP-III protein (AA 1-8...	+3	46	0.59	2
gi 208127	(M88539) Col-CTAP-III (Leu21), small...	+3	46	0.70	2
gi 1685110	(U58210) tetrahydrofolate dehydrogenase	-3	68	0.79	1
gi 791038	(X84709) mediator of receptor induction	+3	51	0.87	2
pir IIA56912	FADD protein - human /gi 809487 (...	+3	51	0.87	2
gb I002001	Sequence 1 from Patent US 4897348...	+3	44	0.91	2
gi 208159	(M11517) connective tissue activator	+3	44	0.92	2
sp P22366 MY88_MOUSE	MYELOID DIFFERENTIATION PRIMARY R...	+3	66	0.95	1
gi 807578	(M19420) unknown protein [Germist...	+1	43	0.98	2
sp P29425 TX26_PHONE	NEUROTOXIN TX2-6 /pir IIS29216 neu...	+1	34	0.99	2
sp P02775 PF4L_HUMAN	PLATELET BASIC PROTEIN PRECURSOR	...	+3	44	0.9998

ER

gi|1718327 (U75698) ORF K13 [Kaposi's sarcoma-associated herpesvirus]

Length = 139

Plus Strand HSPs:

Score = 121 (55.7 bits), Expect = 3.0e-09, P = 3.0e-09
Identities = 31/97 (31%), Positives = 51/97 (52%), Frame = +3

Query: 18 EVIHQVEEALDTDEKEMLLFLCRDVAIDVVPPNVRDILLDILRERGKLSVGDLAELLYRVR 197

EV+ +V L TD++E++LFL + L L+E G+L+ LAE L+R

Sbjct: 5 EVLCEVARLIGTDDREVVLFLNNVFIPQPTLAQLIGALRALKEEGRLTPLAECLFAG 64

Query: 198 RFDLRKIRKMDRKAVETHLLRNPHLVSDYRVLMSI 308

R DIL+ +L +D + +E HL S Y++ + +

Sbjct: 65 RRDLLRDLHLIDPRFLERHLAGTMSYFSPYQLTVLHV 101

ER

gi|1492103 (U60315) MC160L [Molluscum contagiosum virus subtype 1]

Length = 371

Plus Strand HSPs:

Score = 69 (31.7 bits), Expect = 7.4e-06, Sum P(2) = 7.4e-06
Identities = 17/39 (43%), Positives = 24/39 (61%), Frame = +3

Query: 123 DLLDILRERGKLSVGDLAELLYRVRFFDLRKIRKMDRK 239

D L L+ R L++ +AELL +RRFD+LK M R+

Sbjct: 42 DALRALQRRRLTLSSMAELLCALRRFDVLKVRFGMTRE 80

Score = 60 (27.6 bits), Expect = 7.4e-06, Sum P(2) = 7.4e-06
Identities = 12/17 (70%), Positives = 13/17 (76%), Frame = +3

Query: 45 LDTDEKEMLLFLCRDVA 95

LD E E+L FLCRDVA

Sbjct: 18 LDASEHEVLRFLCRDVA 34

Score = 32 (14.7 bits), Expect = 6.8, Sum P(2) = 1.0
Identities = 8/16 (50%), Positives = 10/16 (62%), Frame = +3

Query: 162 VGDLAELLYRVRFFDL 209

V L LL+ V R+DL

Sbjct: 148 VSVLVTLLHAVCRYDL 163

ER

pix|1S55668 hypothetical protein E8 - equine herpesvirus 2 gi|695247

(U20824) ORF E8 [Equine herpesvirus 2]

Length = 171

Plus Strand HSPs:

Score = 66 (30.4 bits), Expect = 4.2e-05, Sum P(2) = 4.2e-05
Identities = 15/34 (44%), Positives = 20/34 (58%), Frame = +3

Query: 120 RDLLDILRERGKLSVGDLAELLYRVRRFDLLKRI 221

RD L + LS + ELL+RV R DL++RI

Sbjct: 39 RDAFKFLSDYACLSAANQMELLFRVGRLDLIRRI 72

Score = 55 (25.3 bits), Expect = 4.2e-05, Sum P(2) = 4.2e-05

Identities = 10/17 (58%), Positives = 13/17 (76%), Frame = +3

Query: 42 ALDTDEKEMLLFLCRDV 92

+LD DE E L+LCRD+

Sbjct: 12 SLDEDETETYLFLCRDL 28

ER

gill1492102 (U60315) MC159L [Molluscum contagiosum virus subtype 1]

Length = 241

Plus Strand HSPs:

Score = 63 (29.0 bits), Expect = 9.5e-05, Sum P(2) = 9.5e-05

Identities = 15/44 (34%), Positives = 25/44 (56%), Frame = +3

Query: 117 VRDILDILRERGKLSVGDLAELLYRVRRFDLLKRIKMDRKAVE 248

V L L ++ KL++ L E+LY ++R DLLK + ++ E

Sbjct: 42 VTQALCSLSQORKLTAAALVEMLYVLQRMDLLKSRFGLSKEGAE 85

Score = 58 (26.7 bits), Expect = 9.5e-05, Sum P(2) = 9.5e-05

Identities = 12/28 (42%), Positives = 16/28 (57%), Frame = +3

Query: -12 SAEVIHQVEEALDTDEKEMLLFLCRDVA 95

S + + E LD+ E +LLFLC D A

Sbjct: 9 SLPFLRHLLEELDSHEDSLLLFLCHDAA 36

ER

gill1813378 (D86547) still life type 1 [Drosophila melanogaster]

Length = 2064

Minus Strand HSPs:

Score = 40 (18.4 bits), Expect = 0.00040, Sum P(4) = 0.00040

Identities = 10/38 (26%), Positives = 17/38 (44%), Frame = -3

Query: 125 VPDIRWNHIYSNIPAQKEQHLLLICIKCFFNLMDDFSR 12

+PD ++ +Y E+ L C + N M+ F R

Sbjct: 1127 MPDNAYSTVYLRDAMSVEEFLASACARRNLNPMEHFVR 1164

Score = 39 (17.9 bits), Expect = 0.00040, Sum P(4) = 0.00040

Identities = 5/11 (45%), Positives = 8/11 (72%), Frame = -3

Query: 299 HQHSIVRNKVR 267

HQH+++ N R

Sbjct: 370 HQHNVINNNTR 380

Score = 35 (16.1 bits), Expect = 0.00040, Sum P(4) = 0.00040

Identities = 8/14 (57%), Positives = 10/14 (71%), Frame = -1

Query: 172 KSPTDSLPLSRKIS 131

+SP DSLP R+ S

Sbjct: 724 RSPWDSLPSLRQDS 737

Score = 33 (15.2 bits), Expect = 0.00040, Sum P(4) = 0.00040
Identities = 7/24 (29%), Positives = 11/24 (45%), Frame = -3

Query: 260 EQVGLHSFSVHLQDTFEQVKSPHS 189

E LH+F L + E + + S

Sbjct: 597 ESYSLHTFEALLSQSMENLANAKS 620

ER

sp|P47211|GALR_HUMAN_GALANIN RECEPTOR (GAL1-R) gi|559048 (L34339)

galanin receptor [Homo sapiens] gi|1297338 (U53511) galanin receptor [Homo sapiens]
Length = 349

Plus Strand HSPs:

Score = 73 (33.6 bits), Expect = 0.31, P = 0.26

Identities = 12/22 (54%), Positives = 15/22 (68%), Frame = +2

Query: 221 LEDGQKSCGDPPAQEPPCFGL 286

L +G SC +PPA EP P FG+

Sbjct: 8 LSEGNASCPEPPAPEPGPLFGI 29

ER

gi|58271 (X12896) CTAP-III protein (AA 1-86) [Cloning vector ps29P]

Length = 86

Plus Strand HSPs:

Score = 46 (21.2 bits), Expect = 0.88, Sum P(2) = 0.59

Identities = 11/31 (35%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVVPPNVRDL 128

EE+LD+D L LC + P N++ L

Sbjct: 8 EESLDSDLYAELRCLCIKTTSGIHPKNIQSL 38

Score = 42 (19.3 bits), Expect = 0.88, Sum P(2) = 0.59

Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA 259

L+DG+K C DP A

Sbjct: 56 LKDGRKICLDPDA 68

ER

gi|208127 (M88539) Col-CTAP-III(Leu21) small fusion protein [Cloning

vector] gi|208129 (M88538) Col-CTAP-III(Leu21) small fusion protein [Cloning vector] gi|209574 (M88536) connective tissue activating peptide III [Cloning vector]

Length = 91

Plus Strand HSPs:

Score = 46 (21.2 bits), Expect = 1.2, Sum P(2) = 0.70

Identities = 11/31 (35%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVPPNVRDL 128

EE+LD+D L LC + P N++ L

Sbjct: 13 EESLDSDLYAEELRCLCIKTTSGIHPKNIQSL 43

Score = 42 (19.3 bits), Expect = 1.2, Sum P(2) = 0.70

Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPAA 259

L+DG+K C DP A

Sbjct: 61 LKDGRKICLDPDA 73

ER

gi|1685110 (U58210) tetrahydrofolate dehydrogenase/cyclohydrolase

[Streptococcus thermophilus]

Length = 284

Minus Strand HSPs:

Score = 68 (31.3 bits), Expect = 1.6, P = 0.79

Identities = 13/40 (32%), Positives = 25/40 (62%), Frame = -3

Query: 284 VRNKVRVP EQVGLHSF SVHLQDTF EQVKSPHS VEQFSQVP 165

VRNK R ++ G HS +V+L ++ + + +E+++Q P

Sbjct: 50 VRNKERA AKKAGFHS KTVNLSE S ISEEELIEVIEKYNQNP 89

ER

gi|791038 (X84709) mediator of receptor induced toxicity [Homo sapiens]

Length = 208

Plus Strand HSPs:

Score = 51 (23.5 bits), Expect = 2.1, Sum P(2) = 0.87

Identities = 14/47 (29%), Positives = 22/47 (46%), Frame = +3

Query: 171 LAELLYRVRRFDLLKRIIKMDRKAVETHLLRNPHLVSDYRVL MSEIG 311

L ELL +RR DLL+R+ + A L + + V+ +G

Sbjct: 63 LRELLASLRRHDLLRRVDDFEAGAAAGA APGEEDLCAAFNVICDNVG 109

Score = 42 (19.3 bits), Expect = 2.1, Sum P(2) = 0.87

Identities = 8/21 (38%), Positives = 12/21 (57%), Frame = +3

Query: 21 VIHQVEEALDTDEKEMLLFLC 83

++H V +L + E L FLC

Sbjct: 7 LLHSVSSSLSSETELKFLC 27

ER

pir||A56912 FADD protein - human gi|809487 (U24231) FADD [Homo sapiens]

Length = 208

Plus Strand HSPs:

Score = 51 (23.5 bits), Expect = 2.1, Sum P(2) = 0.87

Identities = 14/47 (29%), Positives = 22/47 (46%), Frame = +3

Query: 171 LAELLYRVRRFDLLKRILKMDRKAVETHLLRNPHLVSDYRVLMEIG 311
L ELL +RR DLL+R+ + A L + + V+ +G
Sbjct: 63 LRELLASLRRHDLLRRVDDFEAGAAAAGAAPGEEDLCAAFNVICDNVG 109

Score = 42 (19.3 bits), Expect = 2.1, Sum P(2) = 0.87
Identities = 8/21 (38%), Positives = 12/21 (57%), Frame = +3

Query: 21 VIHQVEEALDTDEKEMLLFLC 83
++H V +L + E L FLC
Sbjct: 7 LLHSVSSSLSSSELTELKFLC 27

ER

gb|I002001 Sequence 1 from Patent US 4897348 gb|I101081 Sequence 1 from

Patent WO 8501067

Length = 90

Plus Strand HSPs:

Score = 44 (20.2 bits), Expect = 2.5, Sum P(2) = 0.91
Identities = 10/31 (32%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVVPNVRLD 128
EE+LD+D L +C + P N++ L
Sbjct: 12 EESLDSDLYAELRCMCIKTTSGIHPKNIQSL 42

Score = 42 (19.3 bits), Expect = 2.5, Sum P(2) = 0.91
Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA 259
L+DG+K C DP A
Sbjct: 60 LKDGRKICLDPDA 72

ER

gi|208159 (M11517) connective tissue activating peptide-III [Artificial gene]

Length = 91

Plus Strand HSPs:

Score = 44 (20.2 bits), Expect = 2.6, Sum P(2) = 0.92
Identities = 10/31 (32%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVVPNVRLD 128
EE+LD+D L +C + P N++ L
Sbjct: 13 EESLDSDLYAELRCMCIKTTSGIHPKNIQSL 43

Score = 42 (19.3 bits), Expect = 2.6, Sum P(2) = 0.92
Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA-259
L+DG+K C DP A
Sbjct: 61 LKDGRKICLDPDA 73

ER

sp|P22366|MY88_MOUSE_MYELOID DIFFERENTIATION PRIMARY RESPONSE PROTEIN

MYD88 pir||S11226 MyD88 protein - mouse gi|53294 (X51397) MyD88
protein (AA 1-243) [Mus musculus]
Length = 243

Plus Strand HSPs:

Score = 66 (30.4 bits), Expect = 2.9, P = 0.95
Identities = 17/42 (40%), Positives = 23/42 (54%), Frame = +3

Query: 96 IDVPPNVRDLDLILRERGKLSVGDLAELLYRVRRFDLLKRI 221

++ P R LLD + R SVG L ELL + R D+LK +

Sbjct: 11 LETRPDPTRSLDAWQGRSGASVGRLLLELLALLDREDILKEL 52

ER

gi|807578 (M19420) unknown protein [Germiston virus]

Length = 75

Plus Strand HSPs:

Score = 43 (19.8 bits), Expect = 3.9, Sum P(2) = 0.98
Identities = 5/12 (41%), Positives = 8/12 (66%), Frame = +1

Query: 226 RWTEKLWRPTCS 261

+WT+ WR C+

Sbjct: 42 KWTQNFWRRLCA 53

Score = 39 (17.9 bits), Expect = 3.9, Sum P(2) = 0.98
Identities = 9/22 (40%), Positives = 12/22 (54%), Frame = +1

Query: 142 GKEVSCLSGTWLNCSTE*GDLT 207

G++ +C S L CS E D T

Sbjct: 8 GQKSTCPSSQVLKCSLELSDST 29

ER

sp|P29425|TX26_PHONEUTRIA_NIGRIVENTER TX2-6 pir||S29216 neurotoxin Tx2 -

spider (Phoneutria nigriventer) gi|256377 neurotoxin Tx2-6
[Phoneutria nigriventer=Brazilian armed spiders, venom, Peptide, 48 aa]
Length = 48

Plus Strand HSPs:

Score = 34 (15.6 bits), Expect = 4.3, Sum P(2) = 0.99
Identities = 6/13 (46%), Positives = 8/13 (61%), Frame = +1

Query: 121 GTFWIFYGKEVSC 159

G FWI + K +C

Sbjct: 34 GYFWIAWYKLANC 46

Score = 33 (15.2 bits), Expect = 4.3, Sum P(2) = 0.99
Identities = 6/13 (46%), Positives = 6/13 (46%), Frame = +2

Query: 89 CCYRCGST*CQGP 127

CC G C GP

Sbjct: 16 CCGERGEVCVCGGP 28

ER

sp|P02775|PF4L HUMAN PLATELET BASIC PROTEIN PRECURSOR (PPB) (CONTAINS:

CONNECTIVE-TISSUE ACTIVATING PEPTIDE III (CTAP-III), LOW-AFFINITY PLATELET FACTOR IV (LA-PF4), BETA-THROMBOGLOBULIN (BETA-TG), NEUTROPHIL-ACTIVATING PEPTIDE 2 (NAP-2) .pir||TGHU
beta-thromboglobulin precursor - human gi|181176 (M54995)
connective tissue activating peptide III [Homo sapiens] gi|344294
(A0i319) novel factor having neutrophil-stimulating activity
[unidentified]

Length = 128

Plus Strand HSPs:

Score = 44 (20.2 bits), Expect = 8.5, Sum P(2) = 1.0
Identities = 10/31 (32%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVVPPNVRDL 128

EE+LD+D L +C + P N++ L

Sbjct: 50 EESLDSDLYAEELRCMCIKTTSGIHPKNIQSL 80

Score = 42 (19.3 bits), Expect = 8.5, Sum P(2) = 1.0
Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA 259

L+DG+K C DP A

Sbjct: 98 LKDGRKICLDPDA 110

Parameters:

V=50

B=50

H=0

-filter=SEG

P=4

-ctxfactor=5.61

E=10

Frame	MatID	Matrix name	As Used			Computed		
			Lambda	K	H	Lambda	K	H
Std.	0	BLOSUM62				0.319	0.135	0.396
+3	0	BLOSUM62	0.319	0.135	0.396	0.320	0.140	0.377
+2	0	BLOSUM62	0.319	0.135	0.396	0.376	0.173	0.727
+1	0	BLOSUM62	0.319	0.135	0.396	0.353	0.151	0.594
-1	0	BLOSUM62	0.319	0.135	0.396	0.335	0.143	0.410
-2	0	BLOSUM62	0.319	0.135	0.396	0.350	0.154	0.532
-3	0	BLOSUM62	0.319	0.135	0.396	0.334	0.143	0.458

Query

Frame	MatID	Length	Eff.Length	E	S	W	T	X	E2	S2
+3	0	103	103	10	58	3	13	22	0.11	32
+2	0	104	104	10	58	3	13	22	0.11	32
+1	0	104	104	10	58	3	13	22	0.11	32
-1	0	104	65	10	55	3	13	22	0.11	30
-2	0	104	104	10	58	3	13	22	0.11	32
-3	0	103	103	10	58	3	13	22	0.11	32

Statistics:

Query	Expected	Observed	HSPs	HSPs	
Frame	MatID	High Score	High Score	Reportable	Reported
+3	0	62 (28.5 bits)	121 (55.7 bits)	18	18
+2	0	62 (28.5 bits)	73 (33.6 bits)	7	7
+1	0	62 (28.5 bits)	62 (28.5 bits)	3	3
-1	0	58 (26.7 bits)	50 (23.0 bits)	1	1
-2	0	62 (28.5 bits)	59 (27.1 bits)	0	0
-3	0	62 (28.5 bits)	68 (31.3 bits)	4	4

Query	Neighborhood	Word	Excluded	Failed	Successful	Overlaps	
Frame	MatID	Words	Hits	Hits	Extensions	Extensions	Excluded
+3	0	474	3643889	411910	3212799	19180	7
+2	0	1018	4815505	897825	3908333	9347	34
+1	0	1582	5097249	987386	4099341	10522	8
-1	0	287	1981913	251753	1723979	6181	6
-2	0	656	4186873	555161	3623591	8121	3
-3	0	947	4154885	590204	3549776	14905	7

Database: Non-redundant GenBank CDS translations+PDB+SwissProt+SPupdate+PIR

Release date:

Posted date: 8:09 AM EST

of letters in database: 68,723,500

of sequences in database: 241,922

of database sequences satisfying E: 17

No. of states in DFA: 571 (56 KB) 4

Total size of DFA: 109 KB (128 KB)

Time to generate neighborhood: 0.01u 0.01s 0.02t Real: 00:00:00

No. of processors used: 4

Time to search database: 47.57u 0.34s 47.91t Real: 00:00:12

Total cpu time: 47.64u 0.45s 48.09t Real: 00:00:12

2 6304

DNA Strider™ 1.2

Exhibit G

mmest -> List

DNA sequence 313 b.p. agagtaggatgt ... agagattggta linear

1	10	20	30	40	50	60
1	agagtaggat	gtctgctgaa	gtcatccatc	aggttgaaga	agcaacttgc	acagatgaga
61	aggagatgt	gcttttttgc	tgccggatg	ttgttataga	tgtggttcca	cctaattgtca
121	gggacccct	gatatttttgc	cgggaaagag	gtaaatgtc	tgtcgccgc	ttggctgaac
181	tgcctcacag	agtggggcga	tttgacccgc	tcaaaacgtat	cttggatgt	gacagaaaaag
241	ctgtggagac	ccacccgttc	aggaaaccctc	accccttttc	ggactataga	gtgctgtatgt
301	cagagatgg	tga				300
	10	20	30	40	50	60

Exhibit H

```
>tmpseq1
GTGTGTCTGGTAGCCGAGGATCCCAGAGTGTATGGTGTGGATCAGACTCACTCAGGGCTC
CCTGCATCACATCA
GGAGGATGTTCATGGGAGATTCATGCCCTTATCTAGCAGGGAAAGCCAAAGATGTTTTATTCA
GAACT
ATGTGGTGTCA
AGGGCCAGCTGGAGGACAGCAGCCTCTTGGAGGTGGATGGGCCAGCGATGAAGAATG
```

Exhibit I

[Image]

[progress meter]

Search in progress, please wait for results

BLASTN 1.4.9MP [26-March-1996] [Build 14:27:07 Apr 1 1996]

Reference: Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. J. Mol. Biol. 215:403-10.

Notice: this program and its default parameter settings are optimized to find nearly identical sequences rapidly. To identify weak similarities encoded in nucleic acid, use BLASTX, TBLASTN or TBLASTX.

Query= tmpseq_1
(219 letters)

Database: Non-redundant Database of GenBank EST Division
816,369 sequences; 299,962,672 total letters.

Sequences producing High-scoring Segment Pairs:	High Score	Smallest Sum Probability	
		P(N)	N
gb AA001257 AA001257 zh82c06.r1 Soares fetal liver spleen...	360	1.2e-63	3
gbj C05730 C05730 similar to none	250	4.5e-37	3
gb AA149562 AA149562 zo29e05.r1 Stratagene colon (#937204...)	267	2.1e-33	3
gb T93307 T93307 ye29c04.s1 Homo sapiens cDNA clone 1...	191	2.4e-09	2
gb AA151642 AA151642 zo29e05.s1 Stratagene colon (#937204...)	204	2.0e-07	1

gb|AA001257|AA001257 zh82c06.r1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 427786 5'.
Length = 615

Plus Strand HSPs:

Score = 360 (99.5 bits), Expect = 1.2e-63, Sum P(3) = 1.2e-63
Identities = 72/72 (100%), Positives = 72/72 (100%), Strand = Plus / Plus

Query: 135 TTTTATTCAAGAACTATGTGGTGTCAAGAGGGCCAGCTGGAGGACAGCAGCCTCTTGAGG 194
Sbjct: 529 TTTTATTCAAGAACTATGTGGTGTCAAGAGGGCCAGCTGGAGGACAGCAGCCTCTTGAGG 588

Query: 195 TGGATGGGGCCA 206
Sbjct: 589 TGGATGGGGCCA 600

Score = 353 (97.5 bits), Expect = 1.2e-63, Sum P(3) = 1.2e-63
Identities = 71/72 (98%), Positives = 71/72 (98%), Strand = Plus / Plus

Query: 67 CCTGCATCACATCAGGAGGATGTTCATGGGAGATTCTAGCAGGGAAGCC 126
Sbjct: 460 CCTGCATCACATCAGGAGGATGTTCATGGGAGATTCTAGCAGGGAAGCC 519

Query: 127 AAAGATGTTTT 138
 ||||||| |||
 Sbjct: 520 AAAGATGTNTTT 531

Score = 213 (58.9 bits), Expect = 1.2e-63, Sum P(3) = 1.2e-63
 Identities = 43/44 (97%), Positives = 43/44 (97%), Strand = Plus / Plus

Query: 25 TCCCAGAGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 68
 |||||||||||||||||
 Sbjct: 417 TCCCAGAGTGTATGGTGTGGATCAGACTCACTCAGGGCTCNC 460

Score = 139 (38.4 bits), Expect = 2.2e-57, Sum P(3) = 2.2e-57
 Identities = 35/45 (77%), Positives = 35/45 (77%), Strand = Plus / Plus

Query: 1 GTGTGTGTCCTGGTGAGCCGAGGATCCCAGAGTGTATGGTGTG 45
 ||||||||||||||||| | || ||| | | |||
 Sbjct: 391 GTGTGTGTCCTGGTGAGCCGAGGANNTCCCAGAGTGTATGGTG 435

dbj|C05730|C05730 similar to none
 Length = 521

Plus Strand HSPs:

- Score = 250 (69.1 bits), Expect = 4.5e-37, Sum P(3) = 4.5e-37
 Identities = 52/55 (94%), Positives = 52/55 (94%), Strand = Plus / Plus

Query: 64 CTCCCTGCATCACATCAGGAGGATGTCATGGGAGATTGATGCCCTTATCTAGCA 118
 | ||||||||||||||| ||||||| |||||||||||||||||||
 Sbjct: 467 CCCCTGCATCACATCAGGAAGATGTCNTGGGAGATTGATGCCCTTATCTAGCA 521

Score = 236 (65.2 bits), Expect = 4.5e-37, Sum P(3) = 4.5e-37
 Identities = 48/49 (97%), Positives = 48/49 (97%), Strand = Plus / Plus

Query: 20 GAGGATCCCAGAGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 68
 |||| | ||||||||||| ||||||| |||||||
 Sbjct: 421 GAGGCTCCCAGAGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 469

Score = 120 (33.2 bits), Expect = 4.5e-37, Sum P(3) = 4.5e-37
 Identities = 24/24 (100%), Positives = 24/24 (100%), Strand = Plus / Plus

Query: 1 GTGTGTGTCCTGGTGAGCCGAGGA 24
 |||||||||||||||||
 Sbjct: 399 GTGTGTGTCCTGGTGAGCCGAGGA 422

gb|AA149562|AA149562 zo29e05.rl Stratagene colon (#937204) Homo sapiens
 cDNA clone 588320 5'
 Length = 538

Plus Strand HSPs:

Score = 267 (73.8 bits), Expect = 2.1e-33, Sum P(3) = 2.1e-33
 Identities = 55/57 (96%), Positives = 55/57 (96%), Strand = Plus / Plus

Query: 66 CCCTGCATCACATCAGGAGGATGTTCATGGGAGATTGATGCCCTTATCTAGCAGGGA 122
 Sbjct: 465 CCCTGCATCACATCAGGAGGATGTTCATGGGAGAATGATGCCCTTATCTAGCAGGAA 521

Score = 221 (61.1 bits), Expect = 2.1e-33, Sum P(3) = 2.1e-33
 Identities = 45/46 (97%), Positives = 45/46 (97%), Strand = Plus / Plus

Query: 23 GATCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 68
 Sbjct: 421 GGTCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 466

Score = 135 (37.3 bits), Expect = 1.2e-24, Sum P(3) = 1.2e-24
 Identities = 35/45 (77%), Positives = 35/45 (77%), Strand = Plus / Plus

Query: 1 GTGTGTGTCCTGGTGAGCCGAGGATCCCAGAGTGTGTATGGTGTG 45
 Sbjct: 397 GTGTGTGTCCTGGTGAGCCGAGGAGGTCCCAGAGTGTGTATGGT 441

Score = 75 (20.7 bits), Expect = 2.1e-33, Sum P(3) = 2.1e-33
 Identities = 15/15 (100%), Positives = 15/15 (100%), Strand = Plus / Plus

Query: 126 CAAAGATGTTTTAT 140
 Sbjct: 523 CAAAGATGTTTTAT 537

gb|T93307|T93307 ye29c04.s1 Homo sapiens cDNA clone 119142 3'.
 Length = 294

Minus Strand HSPs:

Score = 191 (52.8 bits), Expect = 2.4e-09, Sum P(2) = 2.4e-09
 Identities = 39/40 (97%), Positives = 39/40 (97%), Strand = Minus / Plus

Query: 190 CAAAGAGGCTGCTGTCCTCCAGCTGGCCCTCTGACACCCAC 151
 Sbjct: 255 CCAAGAGGCTGCTGTCCTCCAGCTGGCCCTCTGACACCCAC 294

Score = 89 (24.6 bits), Expect = 2.4e-09, Sum P(2) = 2.4e-09
 Identities = 21/25 (84%), Positives = 21/25 (84%), Strand = Minus / Plus

Query: 212 TTATCGTGGCCCCATCCACCTCCAA 188
 Sbjct: 234 TCATCGCTGGCCCATCCACCTCCAA 258

gb|AA151642|AA151642 zo29e05.s1 Stratagene colon (#937204) Homo sapiens
 cDNA clone 588320 3' similar to contains Alu repetitive element;
 Length = 608

Minus Strand HSPs:

Score = 204 (56.4 bits), Expect = 2.0e-07, P = 2.0e-07
 Identities = 64/93 (68%), Positives = 64/93 (68%), Strand = Minus / Plus

```
Query: 187 AGAGGCTGCTGTCCAGCTGGCCCTGACACCACATAGTTCTGAATAAAAACATCTT 128
        |||||||          |||||||          |||||||          |||||||          |
Sbjct:  446 AGAGGCTGCTGTCTCAAGCTGGCCCTGACACCACATAGTTCTGAATAAAAACATCT 505
```

Parameters:

V=100
B=50
H=0
P=4

-ctxfactor=2.00
E=1.0

Query			As Used			Computed		
Strand	MatID	Matrix name	Lambda	K	H	Lambda	K	H
+1	0	+5,-4	0.192	0.173	0.357	same	same	same
-1	0	+5,-4	0.192	0.173	0.357	same	same	same

Query											
Strand	MatID	Length	Eff.Length	E	S	W	T	X	E2	S2	
+1	0	219	219	10.	111	11	0	73	0.021	74	
-1	0	219	219	10.	111	11	0	73	0.021	74	

Statistics:

Query		Expected		Observed		HSPs		HSPs	
Strand	MatID	High	Score	High	Score	Reportable		Reported	
+1	0	119	(32.9 bits)	365	(100.9 bits)	11		11	
-1	0	119	(32.9 bits)	204	(56.4 bits)	3		3	

Query	Strand	Neighborhood	Word	Excluded	Failed	Successful	Overlaps
	MatID	Words	Hits	Hits	Extensions	Extensions	Excluded
+1	0	212	26331	2286	22832	1213	1
-1	0	212	23923	2040	20821	1062	5

Database: Non-redundant Database of GenBank EST Division
Release date:
Posted date:
of letters in database: 299,962,672
of sequences in database: 816,369
of database sequences satisfying E: 5
No. of states in DFA: 172 (172 KB)
Total size of DFA: 178 KB (192 KB)
Time to generate neighborhood: 0.00u 0.00s 0.00t Real: 00:00:00
No. of processors used: 4
Time to search database: 9.20u 0.31s 9.51t Real: 00:00:03
Total cpu time: 9.21u 0.32s 9.53t Real: 00:00:03

Exhibit J

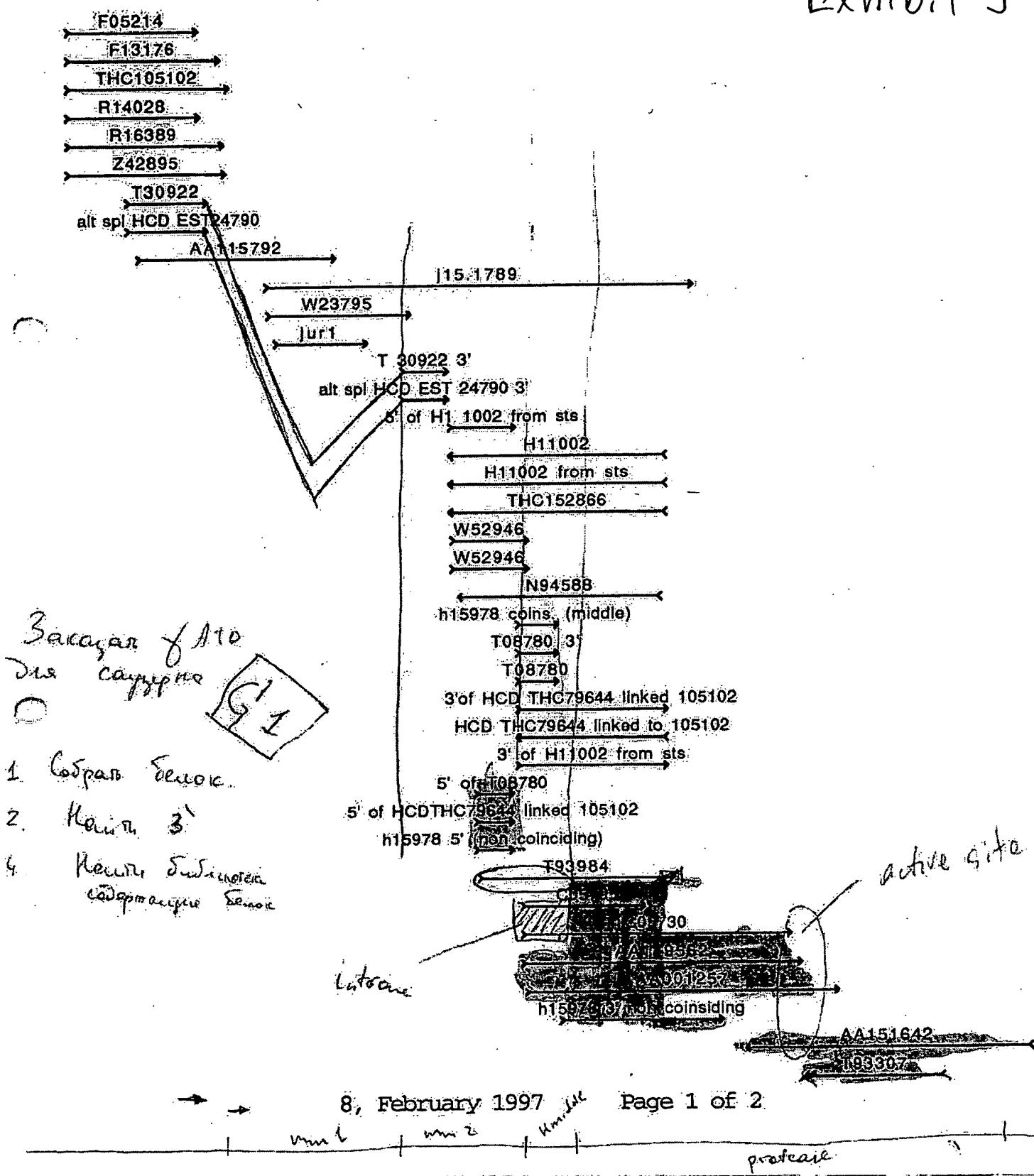


Exhibit K

Oligos for G1

2 - 9 - 1997

for 5' utr sense
5' GTT TCT TTG CCT CCA TCT TGG GTG CGC CTT 3' 18646

fot atg in mm sense
5' ATG TCT GCT GAA GTC ATC CAT CAG GTT GAA 3' 18647

for before middle reg sense
5' CTG GTT GCC CCA GAT CAA CTG GAT TTA TTA 3' 18648

after middle antisense 18649
5' GCC AAG CTG TTC CTT AAG TCT TTG TTC TTT 3'

first strong homology in prot reg (YKMKSK) sense
5' ACC TGA AGA GAG ATA CAA GAT GAA GAG CAA 3' 18650

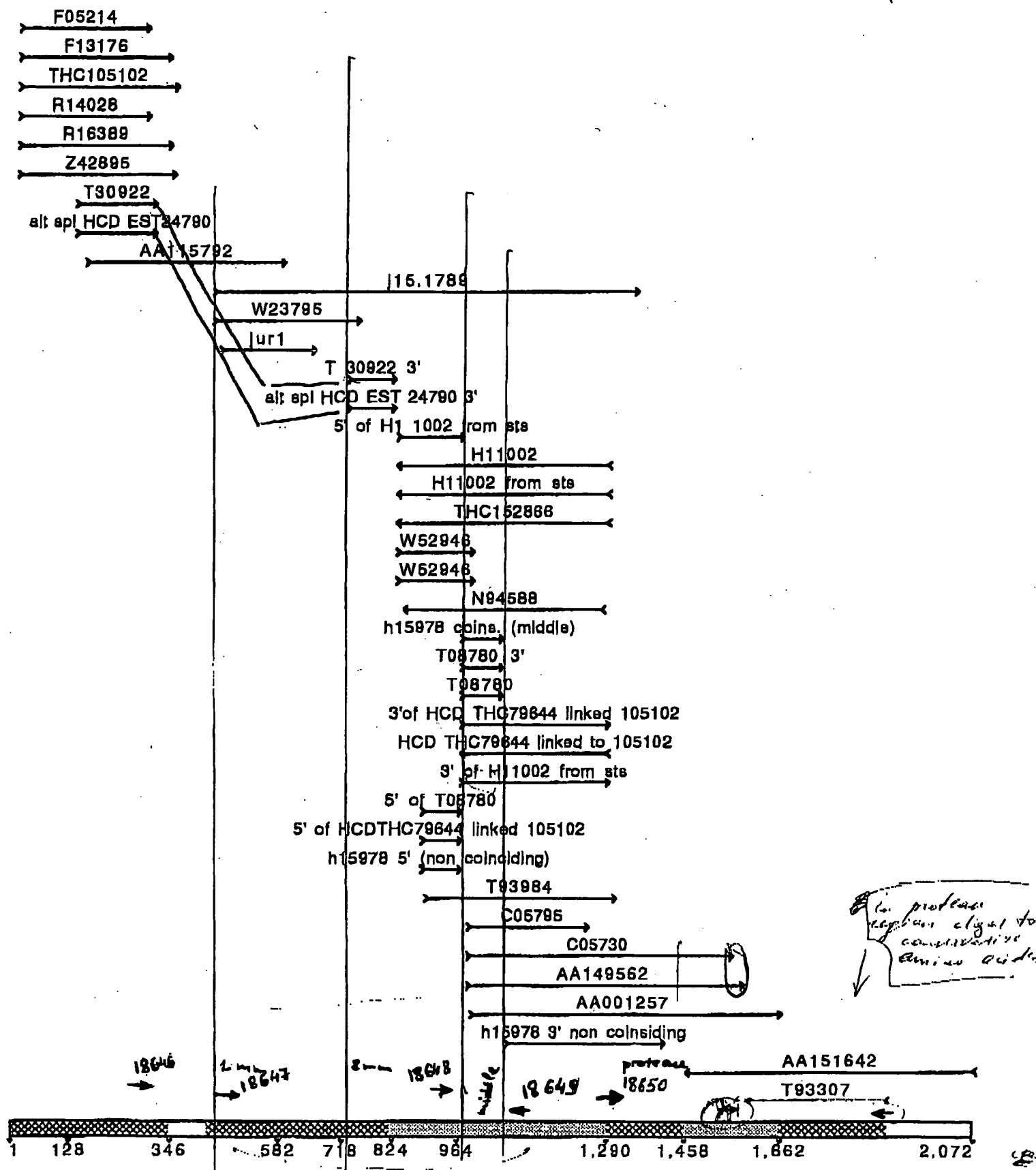
for second subunit for (EADF) antisense
5' CAG TAC ACA GGC TCC AGA AGA AGT CAG CTT 3' 12651

yura

60.5 60.5 60.5

Contig [0020]
Sequencher™ "big contig"

Exhibit L



DATE _____

Sub 1 Sub 2

111

Exhibit M



21

21

3



Vadim
elawer
Cgal

my
PT
elawer
Vd
xwo

13.2.17

PAGE 00

DATE _____

112

1234567891011121314

RI

BNI

pcv1 [→ Xb15ac]

pcv2 (Sb15ac)

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

~~PCV2 Sb15ac~~

1 2 3 4 5 6

② ③ PAB/ADT1/ET

PGBTS_{cat} 1/ET

④ PAB-T1/ET

PAB ② ③ P/BNI

~~Deleba~~ mutants v2

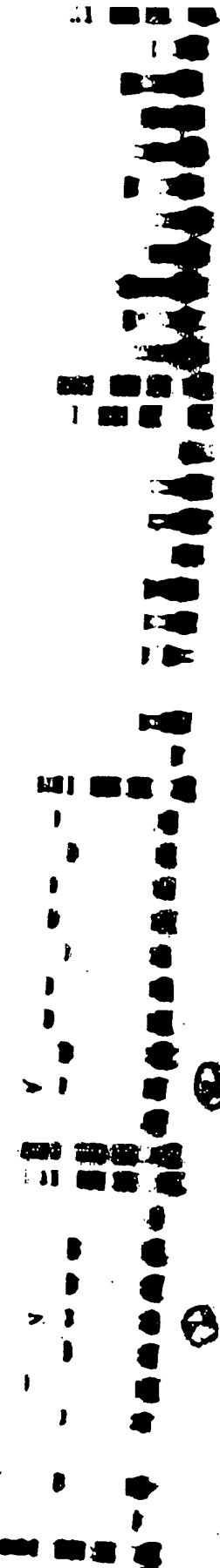


Exhibit N

[Image]

[progress meter]

Search in progress; please wait for results

TBLASTN 1.4.9MP [26-March-1996] [Build 14:27:13 Apr 1 1996]

Reference: Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. J. Mol. Biol. 215:403-10.

Notice: statistical significance is estimated under the assumption that the equivalent of one complete reading frame of the database codes for protein and that significant alignments will involve only coding reading frames.

Query= tmpseq_1
(139 letters)

Database: Non-redundant Database of GenBank EST Division
824,500 sequences; 302,742,428 total letters.

Sequences producing High-scoring Segment Pairs:	Reading Frame	High Score	Smallest Sum Probability	
			P(N)	N
gb AA198928 AA198928 mu23f09.r1 Soares 2NbMT Mus muscu...	+3	79	0.040	1
gb AA014850 AA014850 mh28c10.r1 Soares mouse placenta ...	+1	37	0.81	2
gb W23795 W23795 zb79a05.r1 Soares senescent fibro...	+3	63	0.9997	1

gb|AA198928|AA198928 mu23f09.r1 Soares 2NbMT Mus musculus cDNA clone
640265 5' similar to TR:G695247 G695247 ORF E8. ;
Length = 421

Plus Strand HSPs:

Score = 79 (36.9 bits), Expect = 0.040, P = 0.040
Identities = 25/106 (23%), Positives = 41/106 (38%), Frame = +3

Query: 5 EVLCEVARKLGTDDREVVLFLNNVFIPQPTLAQLIGALRALKEEGRLTPLLAECEXXXXX 64
EV+ +V L D++E++LFL + L +L E G+L+F LAE
Sbjct: 99 EVIHQVEECLDEDEKEMMLFLCRDVTEENLAAPNVRDLDLSLSERGQLSFATLAELLYRVR 278

Query: 65 XXXXXXXXXXXXXXXERHLÄGTMSYFSPYQLTVLHVGDGELCARDI 110
E HL S Y++ ++ + L D+
Sbjct: 279 RF DLLKRILKTDKATVEDHLRRNPHLVSDYRVLLMEIGESLDQNDV 416

gb|AA014850|AA014850 mh28c10.r1 Soares mouse placenta 4NbMP13.5 14.5
Mus musculus cDNA clone 443826 5'
Length = 143

Plus Strand HSPs:

Score = 37 (17.3 bits), Expect = 1.7, Sum P(2) = 0.81
Identities = 9/14 (64%), Positives = 9/14 (64%), Frame = +1

Query: 87 TMSYFSPYQLTVLH 100
T S F P QLTV H
Sbjct: 19 TCSSF*PSQLTVKH 60

Score = 35 (16.3 bits), Expect = 1.7, Sum P(2) = 0.81
Identities = 5/6 (83%), Positives = 6/6 (100%), Frame = +3

Query: 134 CTVWKT 139
CTVW+T
Sbjct: 63 CTVWQT 80

gb|W23795|W23795 zb79a05.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 309776 5'
Length = 313

Plus Strand HSPs:

Score = 63 (29.4 bits), Expect = 8.2, P = 1.0
Identities = 18/54 (33%), Positives = 28/54 (51%), Frame = +3

Query: 5 EVLCEVARKLGTDDREVVLFLNVFIPQPTLAQLIGRALKEEGRLTPLLAE 58
EV+ +V L TD++E++LFL + L L+E G+L+ LAE
Sbjct: 18 EVIHQVEEALDTDEKEMLLFLCRDVAIDVVPPNVRDLDILRERGKLSVGDLAE 179

Parameters:

V=100
B=50
H=0
-filter=SEG
P=4

-ctxfactor=6.00
E=10

Query	Frame	MatID	Matrix	name	As Used	Computed				
					Lambda	K	H	Lambda	K	H
	+0	0	BLOSUM62		0.323	0.138	0.404	same	same	same

Query	Frame	MatID	Length	Eff.Length	E	S	W	T	X	E2	S2
	+0	0	139	118	10.	60	3	14	22	0.058	34

Statistics:

Query	Expected	Observed	HSPs	HSPs	
Frame	MatID	High Score	High Score	Reportable	Reported
	+0	63 (29.4 bits)	79 (36.9 bits)	4	4

Query Frame	Neighborhd MatID	Word Words	Excluded Hits	Failed Hits	Successful Extensions	Overlaps Excluded
+0	0	489	27788736	3256934	24493093	38709

Database: Non-redundant Database of GenBank EST Division
Release date: February 16, 1997
Posted date: 7:38 AM EST Feb 16, 1997
of letters in database: 302,742,428
of sequences in database: 824,500
of database sequences satisfying E: 3
No. of states in DFA: 289 (31 KB)
Total size of DFA: 37 KB (64 KB)
Time to generate neighborhood: 0.00u 0.00s 0.00t Real: 00:00:00
No. of processors used: 4
Time to search database: 86.35u 0.35s 86.70t Real: 00:00:22
Total cpu time: 86.37u 0.39s 86.76t Real: 00:00:22

Exhibit O

your ID: 10609.1818 ** our Ref: SampleB-1818 16
10609.1818.seq Length: 1021 February 25, 1997 21:08 Type: N Check: 5641 ..

1 ACCAAACCAA AAAAAGAGNC CTAGAACTAG TCGGAATTAG GCACGAGGTG
51 TCTGCTGAAG TCATCCATCA GGTTGAAGAA GCACTTGATA CAGATGAGAA
101 GGAGATGCTG CTCTTTTGT GCCGGGATGT TGCTATAGAT GTGGTTCCAC
151 CTAATGTCAG GGACCTTCTG GATATTTAC GGGAAAGAGG TAAGCTGTCT
201 GTCGGGGACT TGGCTGAACT GCTCTACAGA GTGAGGCGAT TTGACCTGCT
251 CAAACGTATC TTGAAGATGG ACAGAAAAGC TGTGGAGACC CACCTGCTCA
301 GGAACCCTCA CCTTGTTCG GACTATAGAG TGCTGATGGC AGAGATTGGT
351 GAGGATTGGA ATAAATCTGA TGTGTCCTCA TTAATTTCC TCATGAAGGA
401 TTACATGGGC CGAGGCAAGA TAAGCAAGGA GAAGAGTTTC TTGGACCTTG
451 TGGTTGAGTT GGAGAAACTA AATCTGGTTG CCCCAGATCA ACTGGGATTT
501 ATTAGAAAAA ATGCCTAAAG AACATCCACA GAATAGACCT GAAGACAAAA
551 ATCCAGAAGT ACAAGCAGTC TGTTCAAGGA GCAGGGACAA GTTACAGGGA
601 ATGTTCTCCA AGCAGCAATC CAAAAGATCT CAAGGATCCT TCAAATAACT
651 TCAGGATGAT AACACCCATGCCATTGTC CTGATCTGAA AATTCTTGGAA
701 AATTGTTCCa TGTGATTAAC ATGGAACCTGC CTCTACTTAA TCNTCTGAAT
751 GATAAATCGT TCNTTTCTA AATGTNTTAT AATGTNTTTA NCCCTTNCTT
801 GTTGCAGGTAT TTTAAATGCT TCCCATCTT TGTTACTACT AATATGCNAT
851 AAATAAAATTC CTTGTNCTCT TAAAAAAAAA AAAAAAAAAA AAAAANTTCC
901 CGCGCCCCCA CNCANGGGG GCCGGTCCCN TCCCNNTTN ANTTTTANT
951 CCNGGCCCCCTT TNCCCNNTN GGGAACCCNT CTTNATCTNA ANGAAACCCC
1001 CNTCCTNCNT GCCNCCCCC C

your ID: 11717.1818 ** our Ref: SampleB-1818 17
11717.1818.seq Length: 1028 February 25, 1997 21:08 Type: N Check: 5259 ..

1 CgATTCTATAg ATCAGGGTTT TCCCCAGTCAC GACGTTGTAA AACGACGGCC
51 AGTGAATTGT AATAcGACTC ACTATAGGGC GAATTGGGTA CCGGGCCCCC
101 CCTCGAGGTC GAGCGGCCGC AGGAATTTTT TTTTTTTTTT TTTTTTTTTT
151 TTTTTTTAA AAAgTACAAG GATATTTATT TTATAGCATT ATTAgTAgTA
201 ACACACACATT GGAAAGCATC TAAACATACA GCAACAANAA AGGGCTAAC
251 ACATTTATAAC ACATTTAgAA AATGAAACAA TTTAACATT CAAAATGATT
301 AATTAAAGGC AgTtCCATNT TAATCACATG GAACAATTTC CAAAATTTT
351 CAAATCAGGA CAATGGGCAT AGGGTGTAT CATCCTGAAT TTATTTGAAG
401 GATCCTTGAA ACTCTTTGG ATTGCTGCTT GGAAACATT CCTGTAACCT
451 GTCCCTGCTC CTTGAACAAA CTGCTTGTAC TTCTGGATTT TTGTCTtCAG
501 GTCTATTCTG TGGATgTTCT TTAGGCATTT TTCTAATAAA TCCAgTTGAT
551 CTGGGGCAAC CAAATTATT TTCTCCAAC CAACCACAAG GTCCAAAAAA
601 CTCTTCTCCT TGCTTATCTT GCCTCGGCCGC ATGTTCCCTT CaTGAGGAAA
651 ATTAATGAGG ACCTTCANAT TTATCCAANT CCTCNCCAAT CTCTGCCATC
701 ACACCTATA TTCCAAAACA AGGTGANGGT CCTGAACANG TGGGTCTCAC
751 ACTTTCTGT CCNCTCCAAA TANTTTGAAC AGGTCAAATC CCTCNTCTGT
801 TAAACATTCA CCANTTCCCN ACACAAACTT ACCCTTCCN TAAAATATCA
851 AAGGTCTGA CTTANGTGAA CCCCTCTATA CCNCTCCCGC CCAAAAAAAC
901 CACCCCTCCC NNCTTCATT CTCTCCCCCG AAGGAAAATC NCAAAACNCT
951 CCAATCCANT ATCCAGATCC TTTTNGGGTT GGGGGGTCTC CCCCCAANAA
1001 NTTANNNCCC NCCTNTTGT TTANCCCC

your ID: 18648.1818 ** our Ref: SampleB-1818 18
18648.1818.seq Length: 1012 February 25, 1997 21:08 Type: N Check: 1701 ..

1 AANANGCCTA AAGAACAtCC ACAGAATAGA CCTGAAGACA AAAATCCAgA
51 AGTACAAgCA GTCTGTTCAA GGAGCAGGGA CAAgTTACAG GAATGTTCTC
101 CAAGCAGCAA TCCAAAAGAG TCTCAAGGAT CCTTCAAATA ACTTCAGGAT
151 GATAACACCC TATGCCATT GTCCTGATCT GAAAATTCTT GGAAATTGTT
201 CCATGTGATT AACATGGAAC TGCCTCTACT TAATCATTCT GAATGATTAA
251 ATCGTTTCAT TTTCTAAATG TGTTATAATG TGTTTAGCCC TTTCTTGTG
301 CTGTATGTTT AgATGCTTTC CAATCTTTG TTACTACTAA TAATGCTATA
351 AAATAAAATAT CCTTGACTT CTTAAAAAAA AAAAAAAA aAAAAAAA
401 AAAAAATTNCC TGCAGGCCGCN CAACCTCAAG GGGGGGCCG GTACCCAATN
451 CGCCCTATAN TNATTCTTAT TACAATNCAC TGGCCGNCGT TTTACAACNT
501 CGTNACTGGG AAAAAACCTN ATCTATNAAT CNTAAATACT GAAAAACCCC
551 GCAATTTCAC TTCAACTGTG CATCGTGCAC CGTCTCAATT TCTTCNTTT
601 ATACNTCGTT TNGCCTCTN TTATNTAACT ATACCCCCN AANTCCAAT
651 CTNGGCCNTG TANCCTCTGA TCTATAAAA TTTTAAATG ACTAAAATAA
701 NTGCCCTT TTTTTGGAC CTNCTTCTCN TGAANTTTNT NACAAAGGCT
751 ATCCAAANCT TGGACTCTNC CCNAAGTTGG TCAATCNCNA ACAGGTGTCG
801 GNTNTCTACC TTNCACAAAAA TTCCACAAAAA AGNAAAGGTC AANCTGGTA
851 ANCTTNTTAA ACTCCAATAC CAATCCTNNN ANTATNATNN TATNATNAAT
901 NATTTAAAAA ANNATNTTAN AATTAAATT GACCTAGGTT AAACAAAATT
951 CAANCCAATA CCNCCGTAGT CNGTCCTNCN GGTAACATAA NCCCTTGACC
1001 CCCCCACGGCC CC

Exhibit P

your ID: rti-651.1831 ** our Ref: SampleC-1831 20
rti-651.1831.seq Length: 765 March 3, 1997 11:26 Type: N Check: 1445 ..

1 CTCCGGTGAA CTGTGCACAG CCCTCGCTTC TGAGCCTTGA ATTCCACATT
51 CTTCATCGCT GGCCCATCCA CCTCCAAgAG GCTGCTGTT CTCAGCTGGC
101 CCTCTGACAC CACATAGTTC TGAATAAAAA ACATCTTGG CTTCCCTGCT
151 AGATAAGGGC ATGAATCTCC CATGAACATC CTCCTGATGT GATGCAGGGG
201 GAGCCCTGAg TGAGTCTGAT CCACACCATA CACACTCTGG GAGCCTCCTC
251 GGCTCACCAg GACACACACa AAGCTGTCGT AGTCTCGGTG CTCGGGCATA
301 CAGGCAAATT GGCCAAGAAT CTGGGATATA CCATGCATAC TGAGATGCAA
351 GAATTCTGG ACTTCATAGC CCAGGGGAAG TGAAAGGTGTC TCGAAgAAGC
401 TCTGTCTCAT TGCCAATGCA ATCGATTATC AGGCAGATTG CTAGGGGCTT
451 GCTCTTCATC TTGTATCTCT CTTCAGGTAT GCTCTGAGGC AAAAAAGCTT
501 CTGATTCCtG AATGGATTTC TTCACTGGTT CTTGTTGAGC GCCAAGCTGT
551 TCCTTAAGTC TTTGTTCTTT ACTTCTCCCA TTATGGAGCC TGAAAGTTATT
601 TgAAGGATCC TTGAgACTCT TTTGGATTGC TGCTTGGAAA ACATTCCGT
651 AACTTGTCCC TGCTCCTTGA ACAGATGCTT GTATCTNGG ANTTTGTCT
701 CAGGTCTANT CTGTGGATGT CTTAGGCAT TTTCTCATAA ATCCACTTGA
751 TTTGGGCACA AATTT

your ID: rt1-648.1831 ** our Ref: SampleC-1831 19
rt1-648.1831.seq Length: 763 March 3, 1997 11:26 Type: N Check: 6251 . . .

1 AAAATGCTAA AGAaCaTCCA CAGAATAGAC CTGAAGACAA AAATCCAGAA
51 GTACAAGCAG TCTGTTCAAG GAGCAGGGCA CAAgTTACAG GAAATGTTCT
101 CCAAGCAGCA ATCCAAAAGA GTCTCAAGGA TCCTTCAAAT AACTTCAGGC
151 TCCATAATGG GAGAAGTAAA GAACAAAGAC TTAAGGAACA GCTTGGCGCT
201 CAACAAGAAC CAGTGAAGAA ATCCATTCAAG GAATCAGAAG CTTTTTGCC
251 TCAGAGCATA CCTGAAGAGA GATACAAGAT GAAGAGCAAG CCCCTAGGAA
301 TCTGCCTGAT AATCGATTGC ATTGGCAATG AGACAGAGCT TCTTCGAGAC
351 ACCTTCACCTT CCCTGGGCTA TGAAGTCCAg AAATTCTTGC ATCTCAGTAT
401 GCATGGTATA TCCCAGATTG TTGGCCAATT TGCCTGTATG CCCGAGCACC
451 GAGACTACgA CAGCTTGTG TGTGTCCTGG TGAGCCGAGG AGGCTCCAg
501 AGTGTGTATG GTGTGGATCA gACTCACTCA GGGCTCCCCC TGCATCACAT
551 CAGGAGGATG TTCATGGGAG ATTCACTGCC TTATCTAGCA GGGAAAGCCAA
601 AGATGTTTT TATTCAGAAC TATGTGGTGT CAGAAGGCCA gCTGGAgAAC
651 AgCACCTCTT GGAGGTGGAT GGCCACCANN AAAATGTGGA ATTCCAGGCT
701 CACAACCAAG GCTGTTGCCA TTTCACGACA AACTGANTTC CTCTGGAACCC
751 TGTGTANGCG GGA

Exhibit Q

your ID: v1-t7.1822 ** our Ref: SampleB-1822 23
v1-t7.1822.seq Length: 775 February 25, 1997 21:05 Type: N Check: 6815 ..

1 TCNTTGGCG CGCTTGTGCA CTGGCCGAGG CGGCCTTTT TTTTTTTTT
51 TTTTTTTTT TTTTTTTTT TTTTTTTTT TTTTTTTTT TTTTTTTGAA
101 GTACAAGGAT ATTTATTTA TAGCATTATT AGTAgTAACA AAAgATTGGA
151 AAGCATCTAA ACATACAGCA ACAAgAAAGG GCTAAACACA TTATAACACA
201 TTTAgAAAAT GAAACgATTT AATCATTCAA AATGATTAAG TAAAGGCAGT
251 TCCATGTTAA TCACATGGAA CAATTCCAA AAATTTCAg ATCAGGACAA
301 TGGGCATAGG GTGTTATCAT CCTGAAgTTA TTTGAAGGAT CCTGAAACT
351 CTTTGGATT GCTGCTTGGAA AAACATTCCCT GTAACTTGTC CCTGCTCCTT
401 GAACAAACTG CTTGTACTTC TGGATTTTG TCTTCAGGTC TATTCTGTGG
451 ATGTTCTTTA GGCATTTTC TAATAAATCC AGTTGATCTG GGGCAACCAA
501 ATTTAgTTTC TCCAACCTCAA CCACAAGGTC CAAgAAAATC TTCTCCTTGC
551 TTATCTTGCC TCGGCCCATG TaATCCTTCN TGANGAAAAT TAATGAGGAC
601 CCTCCNATTATCCTTAAATCC TCCCCAATCT CTGCCATCAN CACTCTATAN
651 TCCGAAACAA GGTGANGGTT CCTGAACAGG TGGGTCTCCC ANCTTTCTG
701 TCCATCTTCC AAANACNTT GAACAGGTCA ATCCCCCNCC CGTTAACAT
751 TCCACCAATT CCNANAAAAC TTACT

your ID: v1.1822 ** our Ref: SampleB-1822 17
v1.1822.seq Length: 821 February 25, 1997 21:05 Type: N Check: 3460 ..

1 GGANC GTCGA GGCATTACAA TCGCGAAACC AAGCCATAGC ATGAAACAGC
51 GAGCTTG CAG CCTCACCGAC GAGTCTCAAC TAAAAGGGAC TCCCGGAGCT
101 AGGGGTGGGG ACTCGGCCTC ACACAGTGAG TGCCGGCTAT TGGACTTTG
151 TCCAgTGACA GCTGAGACAA CAAGGACCAC GGGAGGAGGT GTagGAGAGA
201 AGCGCCGCGA ACAGCGATCG CCCAGCACCA AGTCCGCTTC CAGGCTTCG
251 GTTTCTTGC CTCCATCTTG GGTGCGCCTT CCCGGCGTCT AgGGGAGCGA
301 ACGCTGAgGT GGCAgCGGCa GGAGAGTCCg GCCGCGACAG GACTAACTCC
351 CCCaCTGGAA ACGATTCTGA AAGAAATgAA GTCAGCCCTC ATAAATGAAG
401 TTGACTGCCT GCTGGCTTTC TGTTGACTGG CCCGGAGCTG TACTGCaAGA
451 CCCTNGT GAG CTTCCCTAgT CTAAGAGTAN GATGTCTgCT GAAgTCaTCC
501 ATCAgGTTGA aCAagCCNTG ATNCCGATCA NANNGAGATC CTGCCCTTC
551 TGTGCCGGGG ANGTTNCTAT ANATGTGGTT CCNCCTTANT NTCTGGGACC
601 NTCTGGTATT TTTCACNGNN AACAGGTNCC TNTCTGTCCN GGAATNNGCT
651 NACTNCTCCA CTCAATNANG CGATNTNACC TGCTCNACTT CCTNCNATAT
701 GGACTNNCAT CCTGTGGAAN NCCTTTNCT CATGACCCCT CTCCTTTNC
751 CGTACTNACT ATTNCNCNGC TCAANATTNN TTAAGNNCTG NAANANTCNA
801 TCTTNTTCAT TATTTTGCT C

your ID: v2-t7.1822 ** our Ref: SampleB-1822 24
v2-t7.1822.seq Length: 820 February 25, 1997 21:05 Type: N Check: 4660 ..

1 AAAGAGATGG GATCTTGCTA TATTGCCAG GTTGGTATGC AGTGGCTATT
51 CGTAGGCACA ATCACAGCAT GCTATGACCC TGAACTCCTG GGTCNNAAg
101 ATCCTCCCAC CTCAGCCTCC CaAGTAAC TGAAATNCAGG TACCCACACC
151 CACACCCANC TAATTTTGC ATTTCTACTA GGGACAGCGT TTACCATGTT
201 GGCCAGGCTG GTCTCNAAct CCTGACCTGA AGTGATCTGC CCTCCTTGGC
251 CTCCCAAAGT GCTGGGATTA CAGGCGTGAG CCACTACaCC CACCCTTTG
301 GTTTCTTATG TGTAGGAgAg GATAAGTTTC TTTCTCAGAa TGTGCTGCag
351 CCAGACATaA TATTTCTCCT TGGCAGAAC TNTGCNGTTC CAATCATACA
401 TGTAGCCATT GCANTTCAAT GTGAANATCC ANGAAGTGGG CGTTTCTTT
451 CNAGTCTCNN TTTCTGGGAN ANGCACTNCN NGTACCGGAC NGTGAGCTGN
501 TGAAACTGCT CCATCAGGGA ANGTNTGCA TTACACACGG CTCCATAAAN
551 AAATCNNCTT CCNCGNTGAA AATGTGCACN GCCCTCGCTN CTTNATCCTT
601 GAAATNNNTC TTCCTCATCC TNNGNCCNTC CCCNCAAAAA TGGTGCTGTC
651 TCCCAACTGG CCCCCGAAAC ACATTTCTC NNAATNTCNA NNCNNANGC
701 TCCCTGCCCA TATGGCTNAA NCGCCCGAAC TCCCCTGAAC TAACCTGGGG
751 ACCNCCTNA TTNGNAACTN CCACCCNCC CTNGTACTCT TTGNTCCCTC
801 AATTCAATNAC CTTTANTCC

your ID: v4-t7.1822 ** our Ref: SampleB-1822 25
v4-t7.1822.seq Length: 797 February 25, 1997 21:05 Type: N Check: 6426 ..

1 TCNTTGNCG CGCTTGTGCA CTGGCCGAGG CGGCCTTTTT TTTTTTTTTT
51 TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTTTTTT
101 TTTTTTTTTT TTTTTTTTTT AAAAATTNCA AGGATNTTA TTTTATANCA
151 TTATTAGTAT TAACAAAAAA TTGGAAAGCA TCTAACACATA CAGCAACAAA
201 AANGGGNTAA ACNCNTTATA ACNCNTTAA AAAATGAAAC AATTAAATCN
251 TTCAAAATGA TTAATTNAAG GCAGTNCCAT GTTAATCNCN TGGAACAATT
301 TCCAAAAATT TTCAAATNAG GACAATGGC ATAGGGTNTT NTCNNCCTGA
351 ATTTATTTGA AGGATCCTTG AAACNCTTT GGATTGCTGC TTGGAAAACA
401 TTCCCTGTAAC TTGTCCCTGC NCCTTGAACA AACTGCTTGT NCTTCNGGAT
451 TTTTGTCTNC AGGTCTATTC TGTGGATNTT CTTAGGCAT TTTTCTAATA
501 AATCCNNTTN ATCTGGGGCA ACCAAATTAA TTTTCTCCAA CTCAACCACA
551 AGGTCCAAAA AACTCTTCTC CTTGCTTATC TTGCCTCGGC CCATGTTATC
601 CTTCCCTGAGG AAAATTAATG AGGACCCCTCN AATTTATCCA AATCCCCCA
651 ATCTCTGCCA TCANCACTCT ATANTCCGGG TTTCCNAAT GGTAATGGCC
701 TCAAANGATC CNTATCNANA TGTCCCNAAA TNATCCGGCA AAAAAAAACC
751 CGGGCGNTTC NGTCCCAACG AAANAAAAT TCNAACGGAG GCGGACG

your ID: v4.1822 ** our Ref: SampleB-1822 19
v4.1822.seq Length: 836 February 25, 1997 21:05 Type: N Check: 7807 ..

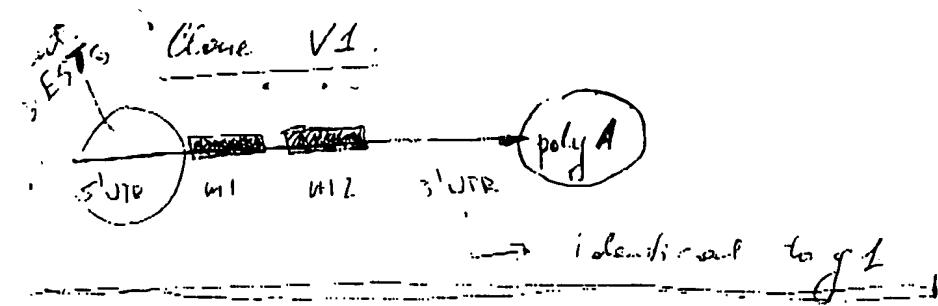
1 GGACCGTCGA GGCCATTACA ATCGCGAAC CGGACTATAG AGTGCTGATG
51 GCAGAGATTG GTGAGGATT GGATAAAATCT GATGTGTCCT CATTAATT
101 CCTCATGAAg GATTACATGG GCCGAGGCAA GATAAgCAAg GAGAAGAGTT
151 TCTTGGACCT TGTGGTTGAG TTGGAGAAC TAAATCTGGT TGCCCCACAT
201 CAACTGGATT TATTaGAaAA ATGCCTACAg AACATCCACA CAATNCACCT
251 GAAgACCaAA ATCCAGAAGT ACAAgCATTG TGTTCAAGGA GCAGGGACaA
301 GTTACCCGAA TGTTCTCCNN TCANCNATCC AAAAGANTCT CANNGGATCC
351 TTCACATAAAC TTCNCGATGA TNACACCCTA NGCCCNTTGT CCTGATCTGA
401 AAANTCTCGG AANTTGTCC ANGTGATTAA CATNGAACTG CCNCTNCNNA
451 NTCANTCTGA ATGACTAAAT CGTTTCACNT CCTNAATGTG TTANANTGTG
501 TNTANCCCCT TCNTGTTGCC TGTATGTCTA CATNCTTCC NNTCNTTCGT
551 TACTNCTANT AATGCTCTNN TATATNTATC CTTGTNCTTC TCTCTCTTCC
601 NCTCCCNCTT CTTCTCTCC TTTCCCTCCCT CCCNCCNTNC TCCCTTCTCT
651 TNCCCTCTCTC TCNNNNCATT AAGGCNCCCC GCTACTTCAA NGGCCCCCAN
701 GGNCCCCNAC ANTNNTTCTT NTTTTTACCC TCCCCCTTNC CCCNNAAGTT
751 GCCCGGTAAN TCCGNCTCCT TANTTTCTN CCCCCCTTCC CCTCNCCCAT
801 CGGAANACTT NNTTATTCG TCTCTCANN NCNNNC

your ID: v5-t7.1822 ** our Ref: SampleB-1822 26
v5-t7.1822.seq Length: 793 February 25, 1997 21:05 Type: N Check: 9524 ..

1 AANTACAAGG ATATTTATTT TATAGCATTA TTAGTAGTAA CAAAAGATTG
51 GAAA^gCATCT AAACATACAG CAACAAGAAA GGGCTAAACA CATTATAACA
101 CATTAGAAA ATGAAACNAT TTAATCATTC AgAATGATTA AGTNNAGGCA
151 GTTCCATGTT AATCACATGG AACAAATTCC AAAAATTTTC AgATCAGGAC
201 AATGGGCATA GGGTGTATC ATCCTGAAgT TATTTGAAGG ATCCTTGAAA
251 CTCTTTGGA TTGCTGCTTG GAAAACATTC CTGTAACCTG TCCCTGCTCC
301 TTGAACAgAC TGCTTGTACT TCTGGATTT TGTCTTCAGG TCTATTCTGT
351 GGATGTTCTT TAGGCATTT TCTAATAAAT CCAgTTGATC TGGGGCAACC
401 AgATTTAGTT TCTCCAACTC AACCCACAAGG TCCAAgAAAA CTCTTCTCCT
451 TGCTTATCTT GCCTCGGCC ATGTAATCCT TCATGAGGAA AATTAATGAG
501 GACACATCAg ATTTATCCAA ATCC^tCACCA ATCTCTGCCA TCAGCACTCT
551 ATAATCCGAA ACAANGTGAA GGTCNTGAA CACGTGGTC TCCACACCTT
601 TTCTGTCCTC TTCAAAATAC TTTGAACAGG TCAATCCCCa CTCTGTAAAC
651 ATTCAACCCAG TCCC^gACNAN NCTTACTCTT TCCNTAAATN CCNAANGTCC
701 NACTTAGTNG AACNCCTTT NCTCCCCGN CCAAAAANCC CCCTCNTCGT
751 TTAATNNTCN CCCC^gANGAG ACNTCCANTC NNCTNACAGG NAC

your ID: v6-t7.1822 ** our Ref: SampleB-1822 27
v6-t7.1822.seq Length: 779 February 25, 1997 21:05 Type: N Check: 1979 ..

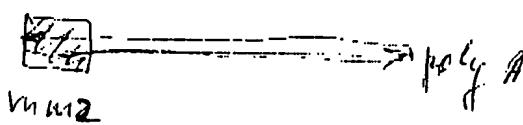
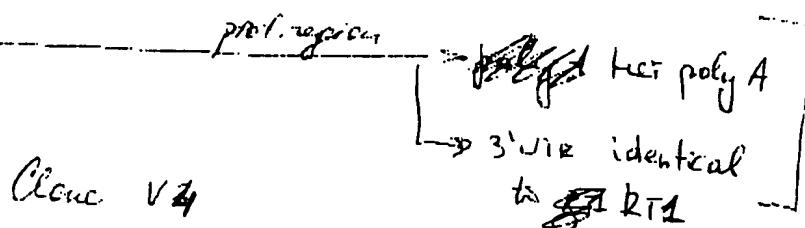
1 GAAgTACAAG GATATTATT TTATAGCATT ATTAGTAGTA ACAAAAGATT
51 GGAAAGCATC TAAACATACA GCAACAAGAA AGGGCTAAC ACATTATAAC
101 ACATTTAGAA AATGAAACgA TTTAATCATT CAgAATGATT AAgTAgAGGC
151 AGTTCCATGT TAATCACATG GAACAATTTC CAAgAATTTC CAgATCAGGA
201 CAATGGGCAT AGGGTGTAT CATCCTGAAG TTATTTGAAG GATCCTTGAg
251 ACTCTTTGG ATTGCTGCTT GGAgAACATT CCTGTAACCT GTCCCTGCTC
301 CTTGAACAgA CTGCTGTAC TTCTGGATT TTGTCTTCAG GTCTATTCTG
351 TGGATGTTCT TTAGGCATTT TTCTAATAAA TCCAGTTGAT CTGGGGCAAC
401 CAgATTTAGT TTCTCCAAct CAACCACAAG GTCCAAgAAA ACTCTTCTCC
451 TTGCTTATCT TGCCTCGGCC CATGTTATCC TTCATGAGGA AAATTAATGA
501 GGACACATCa gATTATCCA AATCCTCACC AATCTCTGCC ATCAGCACTC
551 TATAgTCCGA AACAAAGGTGA AGGTTCTGA ACAGGTGGGT CTCCACAGCT
601 TTTCTGTCCA CTTCAAANAC TTTTGAACAG GTCAATCNCC TCACTCTGTT
651 AAACATTAC CATTCCCGA CAAANNCTTA CTCTTCCCG TNAAATACCN
701 AAAGGTCTG ACATTGTGG AACTCNTCTA TTACACNTCC CGGCNCAAAA
751 AACACNCCNC TTCTCTNNNT TCAATTCT



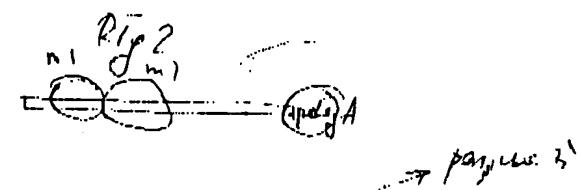
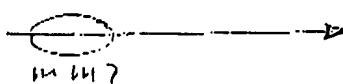
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Exhibit R

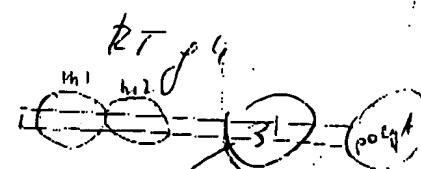
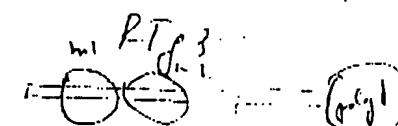
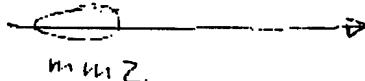
Clone V2



Clone V5



Clone V6



Takao et al. 2000, VL, g1

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oligo 18648

oligo 18649

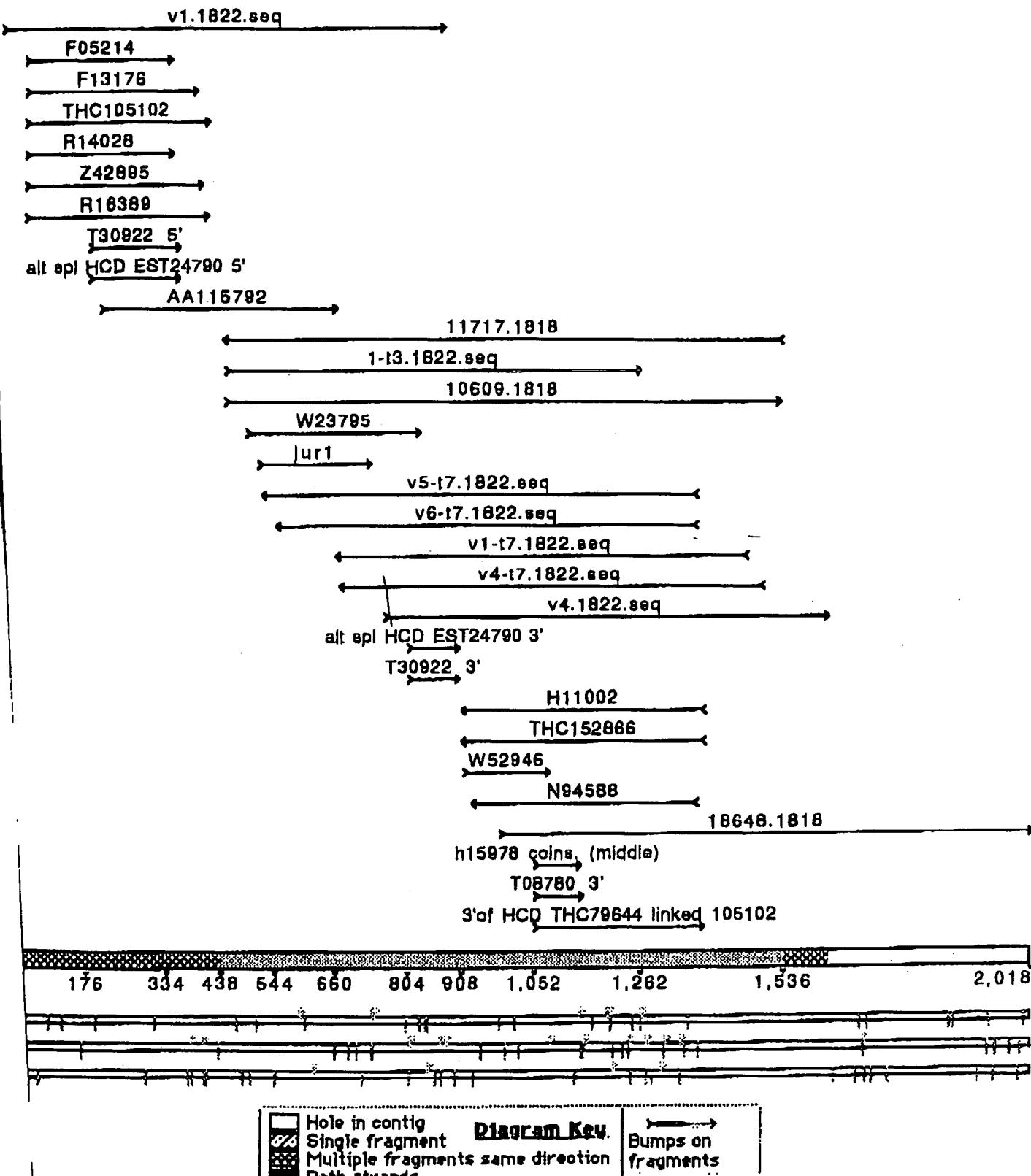
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1-t7.1822.seq

oligo 18651

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Contig [0059]
Sequencher™ "temp oral"

